Dissertation on

A CLINICAL STUDY OF EXUDATIVE AGE RELATED MACULAR DEGENERATION

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CERTIFICATE

This is to certify that the dissertation entitled, **"A CLINICAL STUDY ON EXUDATIVE AGE RELATED MACULAR DEGENERATION"** submitted by **Dr.A.M.RAJA**, in partial fulfillment for the award of the degree of Master of Surgery in Ophthalmology by The Tamilnadu Dr.M.G.R.Medical University, Chennai is a bonafide record of the work done by her in the Regional Institute of Ophthalmology, Government Ophthalmic Hospital, Egmore, Chennai, during the academic year 2007 – 2010.

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CONTENTS

INTRODUCTION

Senile Macular Degeneration was first reported as a clinical entity In 1885 by Otto Haab. He described a variety of pigmentary and atrophic changes in the macular region causing progressive impairment of central vision in patients more than 50 years [6].

Age Related Macular Degeneration is the leading cause of irreversible blindness in individuals over 50 years in developed countries.[4]

DEFINITION

Age Related Maculopathy - is an exaggeration of the normal ageing process characterized by discrete yellow spots at the macula (Drusen) or hyperpigmentation or depigmentation of the RPE associated with drusen [4]

Age Related Macular Degeneration - is a more advanced ,sight threatening stage of ARM characterized by one or more of the following

- Geographic atrophy of the RPE with visible underlying choroidal vessels.
- Pigment epithelial detachment (PED) with or without neurosensory detachment

- Subretinal or sub-RPE choroidal neovascularisation

- Fibroglial scar tissue,haemorrhage and exudates[4]

In the Framingham Eye study, an eye was considered to have AMD if pigment changes,Drusen,retinal changes associated with choroidal neovascularisation in individuals over 50 years of age were thought to be responsible for visual loss to 20/30 or worse , not as a result of cataract or other eye disease.

The definition of AMD should be expanded to include any eccentrically located atrophic or exudative process that would lower visual acuity if it spread into fixation, as well as excessive numbers or confluence of drusen [6]

ANATOMY OF MACULA

Macula is an oval area at the posterior pole measuring about 5 mm in diameter.Its centre is located approximately 4 mm temporal and 0.8 mm inferior to the centre of the optic disc.

Important clinical land marks within the macula are

1. Fovea
2. Foveola
3. Foveal Avascular Zone

Fovea

This is a depression in the inner retinal surface at the centre of the macula.Its diameter is 1.5 mm.Ophthalmoscopically the fovea can be recognized by an oval light reflex arising from the increased thickness of the retina and internal limiting membrane in the parafoveal region.The parafoveal region is the thickest part of the retina containing 6-8 layers of ganglion cells.

Foveola

This forms the central floor of the fovea and has a diameter of 0.35 mm.It is thinnest part of the retina and is devoid of ganglion cells.Its

entire thickness consists only of cones and their nuclei and its subserves the most acute vision.

The umbo is a tiny depression in the very centre of the foveola which corresponds to the ophthalmoscopically visible foveolar reflex seen in most normal eyes.

Foveal Avascular Zone

This measures 0.5 mm in diameter and is therefore situated inside the fovea but outside the foveola .The exact location of the foveal avascular zone can only be determined by FFA.It is a very important landmark I deciding whether or not to treat subretinal neovascular membranes at the macula by laser photo coagulation.

Retinal Pigment Epithelium

This is a single layer of hexagonally shaped cells,the apices of which contain villous process which reach out towards the outer segment of the photoreceptors.The RPE cells in the fovea are taller (11.14 cms) and contains more and larger melanosomes.

Bruchs membrane

This seperates the RPE from the choriocapillaries.On electron microscopy it consists of five elements:

1. Basal lamina of the RPE
2. Inner collagenous layer
3. Middle elastic layer
4. Outer collagenous layer
5. Basal lamina of the choriocapillaries

Changes in Bruchs membrane play an important part in AMD.

Histology of macula

In the fovea and foveola there are no rod photoreceptors ,but only tightly packed cones. All other retinal elements except muller's cells are largely absent.

Despite the displacement of bipolar and ganglion cells to the periphery of fovea, the cones and rods retain their vertical orientation but the inner and outer fibres of photoreceptors are inclined obliquely towards the periphery of macula. The horizontal course of inner photoreceptor fibres forms an external 'Plexiform' lamina-Henle's layer [8]

The annular zone external to the fovea centralis is divided into an inner parafoveal area and an outermost parafoveal area.

The parafoveal region has greatest accumulation of bipolar cells and ganglion cells in the entire retina.

In the perifoveal area the density of cones decreases markedly and outer plexiform layer changes from Henle's layer to a more usual arrangement.

The pigment epithelium and the adjoining chorio-capillary bed are increased over the macular region[8]

The external limiting membrane is pushed inward forming a depression which faces the choroid and has been called the fovea externa.

Normal Aging [6]

It is very relavant to discuss normal aging changes that take place at macula.

Aging is a natural biologic phenomenon, approximately 2-2.5 % of retinal cells may be lost per decade of life. There is no mitosis in these tissues to replace those lost.

- Loss of foveal and foveolar reflexes
- A few small hard drusen are almost always present
- Fine irregularity and increased tigroid nature of the fundus

- Choroidal vessels show clear cut edges and stand out under the macula

Histologically the pigment epithelium show pleomorphism involving size and shape (Friedman,1968).The most notable changes develop at the base of the cells, where there will be deposition of basement membrane material and shedding of membranous debris occur. An increase in lipofuscin content of the Retinal Pigment Epithelium and increase in height of the cell occur .The cone outer segment show increasing disorganization of their normally regular stacked discs dropout of foveal cones. This is followed by an increase diameter of the inner segments of the cones. The outer segment of the rods become convoluted (Marshall et al ,1974)

Bruch's membrane thickening is another constant change in aging. There is associated hyalinization, patchy basophilia (Kinningswoth, 1987). The appearance of debris in Bruch's membrane is due to the build up of lipofuscin in the retinal pigment epithelium.

Basal laminar deposits appear beneath the RPE. Membranous debris appear between strands of basal laminar deposits. It can also be traced through the basement membrane of RPE and the inner collagenous layer of Bruch's membrane. This change as an important bearing on subsequent macular degeneration.

In the choroid there is a loss of middle layer of medium sized vessels. The resulting thinning of the choroid throws the remaining larger vessels into greater prominence, accounting for the senile tigroid fundus.

Epidemiology

AMD is not only the leading cause of blindness in patients over 50 years, it is now also the commonest overall cause of blindness in United states, Canada, England, Australia.

The National Eye Institute estimated that there may be more than 16,000 new cases of legal blindness yearly from this disease. The incidence continues to rise as a result of the increasing percentage of elderly patients. The prevalence of AMD is age related. Framingham eye study estimated that in general population.

Between 52-64 years old incidence was 1.6%

Between 65-74 years old incidence was 6.4%

Between 75 and more years incidence was 30%

Women have higher prevalence rates than men (Liebowitz et al 1980)

RISK FACTORS

Numerous risk factors have been incriminated suggesting that the disease is of multifactorial etiology.

1. Age

The longer one survives, the higher the risk of acquiring the condition. It affects especially persons whose age exceeds the normal life expectancy.

2. Sex

In the Framingham study females out numbered males but this also reflects the increased proportion of females in the older age group.

3. Hereditary factors

Family history of loss of central vision is obtained in about 10-20% of affected individuals.

4. Light ocular pigmentation

One hereditary factor influencing the disease is pigmentation. The incidence of AMD is higher in whites. Individuals with blue irides at risk.AMD is documented to be low in Blacks and Japanese.

5. Cigarette Smoking

An association appears to exist between AMD and cigarette smoking.

6. Hypertension

Conflicting results have appeared for the association between elevated systemic blood pressure and AMD.

But there is definite association with cardiovascular disease.

7. Environmental Factors

AMD may be precipitated or exacerbated by cumulative damage from light toxicity if this exceeds the ability of molecular renewal to restore normal structure. Sunlight has long been suggested as a cause of AMD[13]

8. Role of oxidants antioxidants

Studies from china have shown deficiency of serum zinc. Reports about serum copper levels is not equivocal. Deficiency of serum zinc seems to be a proved factor [10].

9. Other host factors

Attention has to be given to claims of several studies relating AMD to elastotic degeneration of the dermis (Blumenkranz et al) decreased hand grip strength and hypermetropia.

Blumenkranz et al have stressed the association of elastotic degeneration in sun protected skin was predictive of exudative type of AMD[10].

PATHOGENESIS OF ARMD

The RPE, Bruchs membrane and the choriocapillaries must function efficiently to serve as the nutritional complex for the photoreceptors .In a normal eye there are no deposits beneath the RPE.

Basement membrane is not unduly thickened and the choroid consists of the usual three layers of vessels.

In ARMD all these tissues are disturbed, each at one time been regarded as the tissue primarily at fault.

OLD AGE-BRUCH MEMBRANE THICKENS

↓

atherosclerotic changes

↓

Inc.rigidity & dec compliance & increased post.cap resistance

↓

Inc hydrostatic pressure with lipid and protein exudation

↓

DRUSEN

↓

Degeneration of elastin & collagen

↓

Fragmentation of bruch memb

↓

Involutional changes in CC

↓

Inc VEGF

↓

ANGIOGENISIS

Most recent concepts[10]

Dr.Trempe suggests that they are due to degenerative changes occurring at the level of Bruchs membrane and the RPE and this commonly leads to atrophy.

Dr.Jalkh suggests that one of the basic pathogenic factor in ARMD is a break in Bruchs membrane. All the changes that lead to severe visual loss due to ARMD occur after this break in Bruchs membrane.

The CNVM that originate from the choriocapillaries grow under the RPE and retina through this break in Bruchs membrane . The new vessels can be stimulated by factors related to inflammatory reaction involving lymphocytes, active inflammatory cells and tissue growth factors.

TYPES OF ARMD

I . NON NEOVASCULAR / DRY ARMD

The hall mark of DRY ARMD is DRUSEN. Sequlae of DRY ARMD are

- ***Focal hyperpigmentation or atrophy of RPE***
- ***PED***
- ***Geographic atrophy***

II. NEOVASCULAR / WET ARMD

The hall mark of WET ARMD is CNVM. Sequlae of WET ARMD are

- **Hemorrhagic PED**
- **Vitreous hemorrhage**
- **Subretinal disciform scarring**
- **Massive exudation**

Exudative type of AMRD[3]

This type of AMD is the major cause of severe visual loss in the elderly. Only 10% of AMD patients have the exudative form of the disease. In this group legal blindness is 88%.

This exudative form is characterised by the presence of subretinal new vessel which leak serum, blood and lipids. Eventually, this exudative process leads to an organised scar tissue and the cicatric disciform lesion results in a significant and permanent loss of central vision.

Drusen are viewed as anatomical markers of AMD. Focal hyperpigmentation of the RPE and confluent larger drusen were associated with significantly increased risk of exudative disease.

Smiddy and Fine report that 9.9% of patient with bilateral drusen developed exudative form of AMD over a 4 year follow up.

The frequency of developing exudative maculopathy in the second eye ranges 12-43%.

Using Kaplan Meier life table analysis Strahlman *et al* calculated a cumulative risk of 4% at 12 months, 10% at 24 months and 17% at 36 months[6].

Clinical Presentation

- Blurred vision
- Distorted vision most often distorted NV
- Decreased vision
- Micropsia
- Metamorphopsia
- Scotoma

Symptoms arise from subretinal and intra retinal fluid and or blood.

In most cases, the areas of distortion or scotoma can be mapped out on an Amsler Grid.

Choroidal Neovascular Membranes (CNVM)

Clinically CNM appear as a grey green, round, oval irregular lesion. The grey green color might be due to RPE hyper plastic response to CNM. There may be subretinal lipids, haemorrhage with serous or haemorrhagic RPE detachment, sensory retinal detachment.

In a patient who complains of visual loss, metamorphopsia or scotoma of sudden onset, CNM should be suspected. Several clinical signs which suggest the presence of an underlying occult CNVM are:

1. Overlying neurosensory RD
2. Subretinal lipid
3. Chorio retinal folds radiating from the PED.

Immediate FFA should be done to detect any treatable CNM. Careful stereoscopic slit lamp biomicroscopic examination using Hruby lens or 90 dioptre lens may increase the detection rate of CNM.

Histopathologically, a CNM appears as a neovascular sprout growing under or through the RPE via breaks in BM. The endothelial cells in the arborizing neovascular tuft lacks the barrier function of endothelial cells. So the new vessels leak fluid in the neurosensory,

subsensory and subretinal pigment epithelial layer of the retina. The fragile vessels are more prone to haemorrhage. Occasionally the blood may extend through all layers of the retina, breaking through into the vitreous cavity. Ultimately a fibro vascular scar results leading to disruption and death of the overlying retinal tissue and severe visual loss.

CLASSIFICATION OF CNVM

I . Based on location

- **Extrafoveal –** CNV > 200 μm from center to FAZ
- **Juxtafoveal –** CNV 1 – 199 μm from center to FAZ
- **Subfoveal** – under the centre of FAZ

II . Based on FFA

- **Classic CNVM** - well defined early hyperfluorescence with late leakage
- **Occult CNVM** – fibrovascular PED

  - late leakage from undetermined source
- **Predominantly classic CNVM** - classic & occult with classic > 50%
- **Minimally classic CNVM** - classic & occult with classic CNVM < 50%

Retinal Pigment Epithelial Detachments

- Serous retinal pigment epithelial detachments (PED) appear clinically as sharply demarcated, dome shaped elevations of the RPE and overlying neurosensory retina. Neurosensory detachment may be due to an underlying occult CNVM.The causes of PED are

    - **Fibrovascular tissue**
    - **Hemorrhage**
    - **Serous fluid**
    - **Coalescence of drusen**

Haemorrhagic RPE detachment

Bleeding from CNM causes this clinical condition. Appears clinically as round, oval, sharply defined discrete elevation. Blood under RPE appears as dark green or red. Blood may dissect through the edges of detached RPE to subretinal space. Now it is seen as bright red color. Occasionally blood breaks through sensory retina and causes vitreous haemorrhage.

RPE Tears

Also referred to as RPE RIP. This is a known complication of PED. May happen spontaneously or follow laser photocoagulation. Gass suggested than an underlying NVM contributes to RPE tear formation.

When RPE tears, the free edge of the RPE retracts and rolls towards the mound of fibro vascular tissue.

When RPE tear occur at the fovea, it leads to profound loss of vision. Tears occurs at the junction of attached and detached RPE.

In a normal eye, fine basal laminar filaments anchor the RPE firmly to the inner collagenous zone of BM.

In AMD, diffuse thickening of the inner aspect of BM seen clinically as confluent drusen appears to precede spontaneous serous RPE detachments.

The clinical distinction between serous PED and confluent drusen is made on the basis of size and degree of elevation. Lesions larger than 300 um are considered PED.

Disciform Scar

Both treated and untreated cases of choroidal neovascularization may progress to a fibrovascular scar. This involves the choroid, RPE and neurosensory retina. They present as yellow, white hyperpigmented areas. Disciform fibrovascular scar may continue to grow with neovascularization recurring at is edges, invading unaffected areas. Varying degrees of neurosensory fluid, haemorrhage and lipid may overlie the scar.

Disciform scar may masquerade as choroidal tumours when much pigment is seen.

Histopathology reveals few surviving islands of photoreceptors cells. This may explain the better visual performance recorded than would be predicted. As a rule all disciform scar involves the fovea, resulting in severe visual loss.

Break through vitreous haemorrhage

Subretinal haemorrhage may break into the vitreous cavity. The exact mechanism of its occurence is debatable.

In most cases of exudative macular degeneration the peripheral retina remain unaffected. When bleeding occurs through the retina into the vitreous cavity, patients complain of severe and sudden loss of vision involving the peripheral field.

Massive subretinal haemorrhage

Rare complication of exudative AMD. Baba *et al* reported 19% of AMD patients with massive subretinal haemorrhage were on aspirin or warfarin.

FUNDUS FLUORESCEIN ANGIOGRAM

FLUORESCENCE - property of certain molecules to emit light of longer wavelength when stimulated by light of a shorter wave length.

Normal patterns :

1. Choroidal phase
2. Arterial phase
3. Arterio-Venous phase
4. Venous phase
5. Late phase

Choroidal phase (pre arterial phase)

- Normal arm – retina time is 10-12 sec (young), 12-15 sec (old age)
- Dye reachs choroidal circulation through short posterior ciliary artery
- It has shorter course than CRA and enters 1-2sec earlier than retinal circulation

- Early choroidal fluorescence is faint,patchy and irregular scattered throughout the posterior fundus interspersed with scattered islands of delayed filling- **Choroidal flush**

- When areas of choroidal filling and non filling are quite distinct the pattern is called Patchy choroidal filling

- Cilio retinal artery fills in this phase

Arterial phase

- Shows arterial filling and the continuation of choroidal filling

Arterio-Venous phase (capillary phase)

- Complete filling of the arteries and capillaries

- Early laminar flow in the veins in which the dye appears to line the venous wall leaving an axial hypofluorescent strip

Venous phase

- Vascular flow is faster in the center of the vessels than on its side, so dye sticks to the walls of the vein which leads to **Laminar flow**

- Early phase - complete arterial and capillary filling and more marked laminar venous flow

- Mid phase - almost complete venous filling and intensity of venous fluorescence is more than arteries

- Late phase-veins are completely filled and arteries are starting to empty

Late phase

- Small amount of fluorescein entering the retinal circulation after having passed through the kidneys where most of the dye is eliminated

- 10 mts after the injection the vessels of most normal patients are almost completely empty of fluorescein

Fluorescein Angiographic features

Fundus fluorescein angiography is the single most useful diagnostic test in confirming the presence of an exudative lesion. It allows one to determine.

1. The extent of lesion
2. Definition of the lesion
3. Location of the exudative lesion.

These above factors determine the prognostic importance and treatment implications.

Exudative type of AMD - CNVM appear as a discrete, focal area of hyperfiuoresence, first observed before the dye has completely filled the retinal vessels, even during the stage of choroidal filling. Hyperfluorescence increases in both size and degree several minutes later. Fluorescein, may pool in subsensory retinal fluid.

A precise diagnosis and classification system of subretinal neovascularisation in AMD is needed to accurately evaluate the natural history and to select appropriate management [3].

On fluorescein angiography major types of new vessels are at present identifiable.

1. CLASSIC CNVM

Lacy pattern of hyperfluorescence in early phase and increase intensity in mid phase and Leaks in late phase obscuring the boundaries

2. OCCULT CNVM

Speckled hyperflouresence with dye pooled in subretinal space in late phase or late leakage from undetermined source.

This group constitutes more than 50% of CNVMS associated with MD. This may be due to

1. Fluorescence and leakage are blocked by serous detachment
2. RPE detachment
3. Haemorraghic detachment
4. Subretinal blood
5. Turbid fluid and pigment.

Visible SNV can be surrounded or can occur during the natural course, within an area of occult new vessels.

Vascularised pigment epithelial detachments can contain either visible or more frequently subretinal neovascular membrane - which may be partially obscured by turbid or haemorrhagic fluid.

Fluorescein angiography is of major value for the detection and precise location of the neovascular frond in relation to the centre of the foveal avascular zone.

Other types of well defined CNVM

Here CNVM is well defined but leakage is slow and subtle. Leakage may be limited because they may have enough endothelium to prevent leakage when blood flow is slow (Gass, 1985).

In a few patients one may find diffuse ooze without cartwheel or lacy pattern. The geographic borders of well defined neovascular

membranes can be evaluated as they relate to the centre of the foveal avascular zone (the foveola).

This allows to determine and classify subretinal new vessels into 4 groups.

1. Extrafoveal at more than 400 microns from the foveola
2. Juxta foveal between 200 and 400 microns.
3. Juxta foveolar between 5 and 200 microns.
4. Retrofoveolar involving the centre.

Subfoveal new vessels involve atleast 50% of the FAZ and will extend to all the FAZ or beyond. New vessels are either emerging directly under the fovea or growing from an extrafoveal position towards the fovea.

Studies have demonstrated that 54% of visible vessels grow towards the fovea at the rate of 10-18 microns daily in a three-week period.

More than 73% of extra foveal new vessels extend to a subfoveal location after one year.

Among membranes invading all the FAZ three types can be considered.

1. Originating directly in the centre and limited to the FAZ.
2. Larger and involving all the macular areas.
3. Even more extensively to the entire posterior pole.

Lesions of the retinal pigment epithelium detachment

FFA shown rapid uniform fluorescence under the entire dome of the detachment. The dye does not leak beyond the margins of the detachment as the integrity of RPE and tight junctions between adjacent RPE/zonula occludens are intact still. However Bird hypothesis differ. He believes entry of the dye from choroid to sub RPE space is due to concentration gradient rather than due to fluid flow. Atypical features should not be missed. Clinical and angiographic features are :

1. Notch sign, flattening, indentation of margin of detached RPE.
2. Irregular or slowly filling RPE detachment
3. Yellow subretinal exudate, haemorrhage at margins of RPE detachment.
4. Radial chorioretinal folds surrounding RPE detachment.
5. Also serous detachment of sensory retina.

RPE Tears

FFA reveals a zone of choroidal hyperfluorescence due to lack of RPE and a zone of blocked choroidal fluorescence due to doubling of RPE layer as a result of rolling of RPE on itself.

Haemorrhagic RPE detachment

FFA shows a variety of pictures, may be slowly filling, partially blocked fluorescence. Some cases may show hot spot.

INDOCYANINE GREEN ANGIOGRAPHY (ICG)

ICG is very much helpful in studying the choroidal circulation. The Occult CNVM is easily identified with ICG as a focal hyperfluorescent **'hot spot'**, a plaque or a combination of both.

ICG IN CNVM

1. Occult or poorly defined CNV
2. Distinguishing serous from vascularised portion of fibrovascular PED
3. CNV associated with overlying hemorrhage, pigment or exudate
4. Recurrant CNV adjuvent to an old photocoagulation scar

OPTICAL COHERENCE TOMOGRAPHY

Principle of OCT

Optical Ocoherence tomography is based on the principle of Michelson interferometry. Low coherence infra red light coupled to a fibre-optic travels to a beam – splitter and is directed through the ocular media to the retina and to the reference mirror respectively. Light passing through the eye is reflected by structures in different retinal layers. The distance between the beam splitter and the reference mirror is continuously varied. When the distance between the light source and the retinal tissue is equal to the distance between the light source and the reference mirror, the reflected light from the retinal tissue and reference mirror interacts to produce a interference pattern .The interference pattern is detected and then processed into a signal.

The signal is analogous to that obtained by a A-scan ultrasonography using light as a source rather than sound. A two-dimensional image is built as the light source is moved across the retina. The image is in the form of a series of stacked and aligned A-scans, which produces a two-dimensional cross-sectional retinal image that resembles that of a histology. Digital processing aligns the A-scans to

correct for eye motion. Digital smoothing techniques are used to further improve the signal-to-noise ratio.

NORMAL OCT SCAN

On a normal 10mm horizontal scan passing through the fovea, one can clearly demarcate two major landmarks, namely the optic disc and fovea.

The optic disc is seen towards the right of the tomogram can be easily identified by its contour. The central depression represents the optic head cup and the stalk continuing behind is the anterior part of the optic nerve. The fovea is seen towards the left of the tomogram and can be easily identified by characteristic thinning of the retinal layers. The vitreous anterior to the retina is non-reflective and is seen as a dark space. The interface between the non-reflective vitreous and backscattering retinal layers is the vitreoretinal interface.

Retinal morphology and the macular OCT imaging correlate well, with alignment of areas of high and low reflectively to specific retinal choroidal elements.

Resolution of retinal structures by OCT depends in the contrast in relative in reflectivity of adjacent structures.

The nerve fiber layer and ganglion cell layers are reflective, and are seen as bright colors on the false color map. The nuclear layer appear hyporeflective, while the interconnecting plexiform layers and axonal layers are reflective hyper-reflective. Typically the photoreceptor appear slightly hyporeflective compared with the outer retinal layers. The retinal pigment epithelium – choriocapillaries complex is seen as hyper – reflective band. The retinal blood vessels within the neurosensory retina show backscatter and also cast a shadow behind. The choroid is also highly reflective, although it is frequently not well resolved because of light reflection by the overlying retinal pigment epithelium.

OCT in CNVM

1. Disease categorization – OCT gives an insight into the localization of pathology with changes occurring at the ultrastructural level that helps in categorizing the disease.

2. Early occult CNVM – In patients with soft confluent drusen, occult CNVM can often be missed on FFA.

3. Associated changes – OCT helps in depicting additional features like CME ,RPE rip, Neurosensory atrophy of retina.

4. To r/o the presence of underlying CNVM in patients with haemorrhagic PED.

5. Response to treatment – OCT helps in monitoring response to photo coagulation, Transpupillary Thermo Therapy (TTT), Photo Dynamic Therapy (PDT).

MEDICAL TREATMENT

Exudative type of AMD[7]

1. Laser photocoagulation
2. Anti VEGF agents
   - Pegaptanib Na (Macugen**)**
   - Bevacizumab (Avastin)
   - Ranibizumab (Lucentis)
3. Photo Dynamic Therapy (Verteporfin)
4. Pupillary Thermotherapy
5. Anecortave acetate

LASER PHOTO COAGULATION

Historical Interest

Zweng and associates used the Ruby laser to photocoagulate 20 cases of AMD. They found no improvement in visual acuity in advanced cases but felt that laser photocoagulation in early cases might delay the progress of the disease.

Watzke and Snyder employing Zenon photocoagulation demonstrated that it had definite value in early haemorrhagic disciform degeneration.

Laser Treatment of well defined extrafoveal choroidal neovascular membranes [6] (CNVM)

The macular photocoagulation study (MPS) demonstrated that intense Argon blue-green laser photocoagulation treatment of extrafoveal CNVM significantly improved the visual prognosis as compared with the natural course of the disease.

In this study eyes with a discrete extrafoveal CNVM and a baseline visual acuity of 20/100 or better were assigned to treatment. Intense Argon blue-green laser photocoagulation were applied to obliterate the CNVM. At 18 months following laser photocoagulation reduced the risk of severe visual loss from 69% in untreated eyes to 25% in treated eyes.

Disadvantages

1. Three year follow up revealed that 47% of treated eyes versus 62% of untreated eyes progressed to severe visual loss.

2. Recurrence of choroidal neovascularisation was responsible for most of the deterioration.

3. Treatment appears to delay the onset of severe visual loss by 18 months.

4. Membranes within the FAZ and extrafoveal membranes extending into the FAZ were excluded.

Krypton red laser allows one to treat within the foveal avascular zone. There is less risk of damage to the fovea as a result of lack of uptake by the foveal xanthophyll. Also krypton laser spares the inner retina.

The National Eye Institute supported, Krypton Macular photocoagulation study and Foveal photocoagulation study are currently evaluating patients with NVM's within the FAZ.

In cases of poorly defined NVM, the patient is followed at frequent intervals with fluorescein angiography in the hope that the membrane will become well defined.

Principles of Photocoagulation

Photocoagulation destroys the CNVM by heat. Laser light is absorbed by RPE, choroid and converted to heat which gets dissipated to adjacent tissues (Gass, 1981).

RPE proliferation may also be a vital factor. Another theory proposes that laser treatment cause RPE to envelop CNVM and absorb the fluid overlying the CNVM (Miller, 1986).

Laser may cause RPE proliferation as well as RPE derived inhibitors of neovascularisation. At time laser can cause total eradication of CNVM's.

Preparation for treatment

1. Patient should be informed that laser treatment will create a permanent blank area corresponding to the retina destroyed.

2. Laser treatment may cause haemorrhage or increased neurosensory detachment.

3. Laser treatment might actually stimulate new vessel growth in few cases.

4. The ophthalmologist must emphasize to the patient that laser treatment is not a cure for macular degeneration. Laser treatment is designed to

obliterate the neovascular complex and reduce the risk of severe visual loss.

Procedure

1. FFA performed less than 72 hours before treatment. Ideally the angiogram should be less than 24 hours old.

2. Projecting the angiogram on laser console top behind patients head is useful.

3. A drawing of the choroidal NVM and its relationship to the FAZ made.

4. The NVM perimeter, the FAZ and the key land marks around the membrane such as retinal vessels and subretinal blood are drawn.

5. In MPS, retrobulbar anaesthesia was suggested to facilitate treatment.

MPS Photocoagulation Technique

1. With the use of 200 um spot size and duration of atleast 0.2 second, a test burn is placed along the membrane perimeter.

2. The foveal edge of the CNVM is treated next, with overlapping burn of 200 um of 0.2-0.5 seconds. The burns should be sufficiently intense to obliterate the CNVM.

3. Then the rest of the membrane is outlined.

4. Finally the centre of CNM is treated and obliterated.

5. MPS protocol requires the whole treated area should look uniformly intense white, extending 100 um beyond the angiographically visible CNM.

6. Retinal vessels should be avoided.

7. Choroidal haemorrhage is an occasional complication.

8. While treating CNVM temporal to the optic DISC, MPS protocol says 1-2 clock hours of Papillo macular bundle be preserved.

9. Treatment should never extend within 100-200 um from the disc.

Post Treatment Care

1. Ideally FFA should be taken immediately following treatment to check the adequacy of photocoagulation
2. By comparing with pretreatment angiogram one can detect inadequacy of treatment.
3. If need be additional treatment may be given.
4. Usually first post operative examination is after 2 weeks. Later patients are examined at regular intervals of weeks - months.
5. Each time FFA is done to detect any early CNVM recurrence.

6. Visual acuity stabilizes around 6 months in successfully treated eyes.

7. Visual acuity may decline several years after treatment with enlargement of the treatment scar.

Recurrences

Despite adequate photocoagulation, treated eyes are at high risk for persistence of neovascularisation. The MPS reported that recurrent neovascularisation was present in 42% of treated eyes by 12 months and 52% of eyes by 24 months. Eyes with recurrences progressed to severe visual loss. Retreatment of persistent or recurrent neovacularisation should be undertaken when the vessels are located outside the FAZ.

In MPS, CNVM recurrence was associated with cigarette smoking.

Complications of treatment

1. Choroidal haemorrhage - to avoid, it guidelines are to avoid 50 microns spot size and exposure time less than 0.2 seconds.

2. Localised field defects.

3. Macular pucker - This is due to internal limiting membrane contraction.

4. Occlusion of retinal vessels.

ANTI-VEGF AGENTS

Stimulus for increased VEGF expression

- Reduction in choriocapillary blood flow
- oxidative stress
- Alteration in the Bruchs membrane
- Accumulation of the lipids

MOA of VEGF

It binds with flt1 and KDR receptors present in endothelial cells and increased vascular permeability and angiogenesis. Six types isoforms are VEGF 121,145,165,183, 189, 206

MACUGEN (PEGAPTANIB) - VISION TRIAL

Pegylated aptamer of VEGF that selectively block VEGF 165 , Pegylation increases half life and stability

- Used in glaucoma patients
- Dose-0.3mg
- No benefit in occult CNV & lesions more than 4DD.

FDA- approved in 2004

BEVACIZUMAB (AVASTIN)

Bevacizumab (Avastin, Genentech) is a full-length, humanized, murine monclonal antibody directed against all the biologically active forms of vascular endothelial growth factor-A (VEGF). Bevacizumab, the first anti-VEGF drug to be approved by the Food and Drug Administration, was developed as an intravenous therapy for cancer patients because VEGF is one of the major angiogenic stimuli responsible for neovascularization in tumors. Anti-VEGF therapy has shown promising results in several forms of cancer, but the drug is currently approved only for the treatment of metastatic colorectal cancer. When used in cancer therapy, bevacizumab is infused at a dose of 5 mg/kg every two weeks until the patient dies or significant disease progression is observed. In clinical trials, the most common adverse event caused by bevacizumab was hypertension.

Systemic Bevacizumab

The role of VEGF in neovascular AMD has now been confirmed as the result of the Phase III clinical trial of the anti-VEGF drug pegaptanib sodium (Macugen, Eyetech). Pegaptanib sodium is now approved for the treatment of all neovascular AMD; however, the average pegaptanib-treated patient still continues to lose vision while receiving therapy.

Another anti-VEGF drug known as ranibizumab (Lucentis, Genentech) was shown to improve visual acuity, angiographic and optical coherence tomography outcomes in open-label, uncontrolled Phase I/II studies. Genentech's one-year, Phase III results confirm earlier studies in AMD patients. Patients with predominantly occult macular neovascularization treated with ranibizumab had an overall vision improvement and statistically significant better outcomes than the sham-injected controls. The disadvantages of systemic therapy, however, include systemic exposure to an antiangiogenic drug at therapeutic levels, resulting in a higher risk of systemic adverse events compared to intravenous injection.

SANA STUDY

In the spring of 2004, Systemic Avastin for Neovascular AMD (SANA) study at the Bascom Palmer Eye Institute. In this study systemic bevacizumab was offered as salvage therapy for patients who were not candidates for verteporfin photodynamic therapy or who refused PDT. Pegaptanib sodium was not yet commercially available. Unlike the regimens used in cancer therapy, treating patients only two or three times followed by a period of close observation was proposed, with retreatment possible if the leakage from the neovascularization recurred. Since this article was published, a total of 18 patients have been followed for at least 24 weeks, and the 24-week results confirm and improve upon the pre-

liminary results observed at 12 weeks (submitted for publication). Of the 18 patients, nine initially received three treatments, and 11 received only two treatments. The majority of patients did not require another treatment through 24 weeks.

With improvement in visual acuity, OCT and angiographic outcomes, the systemic use of bevacizumab appeared to be both effective and durable. Moreover, the cost of intravenous bevacizumab therapy is comparable to the cost of pegaptanib therapy. The average drug cost for bevacizumab is $2,200 per infusion, and the cost for the 24 weeks of therapy is $4,400 for most patients, roughly equivalent to four intravitreal injections of pegaptanib over 24 weeks.

Intravitreal Bevacizumab

Bevacizumab was used as an intravitreal injection in humans in any of the early clinical studies. The preclinical data in primates suggested that intravitreal bevacizumab would be too large to penetrate the retina and result in any therapeutic effect, but bevacizumab was never tested in an animal model of macular neovascularization to see if this assumption was correct. Once we observed the dramatic results of systemic intravenous bevacizumab in patients with neovascular AMD, a much lower dose of bevacizumab injected into the eye could result in a similar benefit while reducing the risk of systemic adverse events. It has been

calculated that a dose of about 1 to 1.5 mg of bevacizumab would be approximately 400-fold less than the systemic dose of bevacizumab used in the SANA study.

Another appealing feature of intravitreal bevacizumab is its low cost. Compared with the cost of pegaptanib sodium, an intravitreal dose of bevacizumab would be a bargain. While a dose of pegaptanib (0.3 mg) is approximately $1,000 or $3,300 per mg, the proposed 1-mg dose of bevacizumab would cost $5.50. Moreover, a dose of 1 to 1.25 mg could be conveniently injected using 0.04 ml to 0.05 ml of the commercially supplied bevacizumab, which is not known to contain preservatives or additives that may be toxic to the retina. At the Bascom Palmer Eye Institute, off-label intravitreal bevacizumab was offered to patients as a salvage treatment for those who continue to lose vision associated with neovascular lesions and worsening OCT profiles despite treatment with approved therapies. In the first report of a patient receiving intravitreal bevacizumab, improvement in angiographic and OCT outcomes after one injection were observed, nearly identical to the outcomes that observed following systemic bevacizumab and intravitreal ranibizumab. The patient's vision remained stable over four weeks, and this patient has remained stable through six months and has not required another injection.

INTRAVITREAL INJECTIONS–PROCEDURE GUIDELINES

Injection procedure guidelines include consideration of pre existing conditions such as active external infection, eyelid abnormalities, povidone iodine, lid scrubs, pre injection topical antibiotics, lid speculum, drape, gloves, and anaesthesia and post injection topical antibiotics.

In general the risk of endophthalmitis following intra vitreal injection is estimated to be approximately < 0.1%.

Guidelines for intra vitreal injection

1. Povidone iodine for ocular surface, eyelid and eye lashes
2. Use of speculum and avoid contamination of the needle with eye lid margin
3. Avoid extensive massage of the eye lids either pre or post injection
4. Dilate pupil
5. Adequate use of anaesthetic (topical drops/ sub conjunctival injection)
6. Avoid prophylactic or post injection paracentesis
7. IOP to be checked following injection

8. Dilated fundoscopic examination should be performed following injection to confirm central retinal artery perfusion and intra ocular location of the drug.

Guidelines for follow up

Patients should be followed up on the immediate day following intra vitreal injection. However patients should be instructed to contact ophthalmologist if there if increased ocular redness or discomfort or decreased vision compared to that present right after the injection procedure.

LUCENTIS (RANIBIZUMAB)

It is a recombinant humanized monoclonal antibody and binds to all isoforms of VEGF

Dose- 0.5mg.It is used in minimally classical and occult CNV.

PHOTO DYNAMIC THERAPHY (PDT)

Principle

Injection of photosensitizing drug followed by applying light of particular wave length to incite a photochemical reaction

Mechanism

Oxygen free radicals, platelet activation & thrombosis → occlusion of pathological vasculature

Indication

1. Predominantly classic CNV (TAP study)
2. Occult / minimally classic CNV with recent disease progression (VIP study)

Procedure:

- VERTEPORFIN -6mg/kg bw followed 5 min later by application of diode laser for 83 sec.
- 5 to 6 session 3 monthly interval over a period of 2yr before disease stabilise.

ANECORTAVE ACETATE (RETANNE)

- Derivative of cortisone with predominantly angiostatic effect.
- Delivered behind the eye not within the eye .
- No intra ocular complication .

TRANS PUPILLARY THERMOTHERAPY (TTT)

- Subfoveal CNV is slowly heated with diode laser to occlude cnv complex with single laser spot.
- Less damage to overlying retina
- Large Spot size 0.8 – 3 mm
- Long exposure- 1 min
- Power – 400-800 mW
- Low irradiance
- Wave length 810 nm

AIM OF THE STUDY

1. To study the various FFA patterns of exudative ARMD
2. To study the role of OCT in diagnosing and monitoring the treatment response
3. To evaluate the change in visual acuity, macular thickness, angiographic patterns following intravitreal injection of bevacizumab.
4. To assess the systemic risk factors for exudative ARMD.

MATERIALS AND METHODS

This study was done in Retina clinic – Regional Institute of Ophthalmology and Government Ophthalmic Hospital, Chennai during the period of June – 2007 to November – 2009.

INCLUSION CRITERIA

CNVM attributable to ARMD diagnosed by FFA and OCT with BCVA of less than 6 / 24.

EXCLUSION CRITERIA

1. Non exudative ARMD
2. High myopia
3. Chronic uveitis
4. Not associated with other ocular conditions like Diabetic retinopathy, Hypertensive retinopathy
5. Mature cataract

MATERIALS USED

Vision in both eyes were tested using Snellen`s visual acuity chart. Other materials used were

1) Direct ophthalmoscope
2) Indirect ophthalmoscope
3) Slit lamp examination with +90D lens
4) Schiotz and Goldmann applanation tonometer
5) Goldmann 3 mirror
6) Topcon fundus camera
7) Optical coherence tomography
8) Fundus flourescein angiography
9) Blood pressure
10) Urine-albumin sugar

Complete ocular examination was done

a. Best corrected visual acuity

b. Intraocular pressure

c. Anterior segment examination

d. Visual fields

e. Fundus examination – pupil was dilated with 1% Tropicamide eye drops, fundus examination was done with Direct ophthalmoscope, Indirect ophthalmoscope, slit lamp with +90D lens and Goldmann 3 mirror.

f. Fundus photograph was taken with Topcon fundus camera

g. Fundus flourescein angiography was done in cases with 3ml of 20% Sodium flourescein injection IV in dorsal vein of hand with patient seated in front of fundus camera

h. Optical Coherence Tomogram was done (OCT) for all patients.

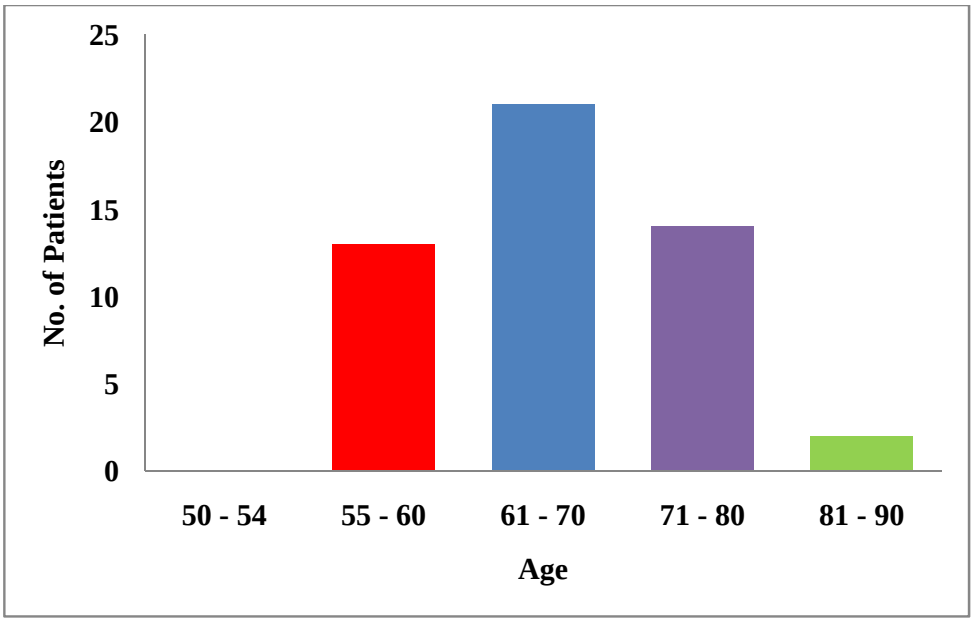
i. A commercially available bevacizumab (1.25mg/0.05ml) was prepared for each patient and placed in a tuberculin syringe using aseptic techniques. After the eye had been prepared in a standard fashion using 5% povidone iodine and topical antibiotics, 1.25 mg (0.05 ml) of bevacizumab was injected intravitreally via the pars plana. After the injection, intraocular pressure and retinal artery perfusion were checked, and patients were instructed to administer topical antibiotics for 3 days. Patients were called 2 to 3 days after injection and were re examined within 1 week.

j. All the patients were asked for regular follow-up at 2weeks, 4 weeks, 8weeks, 12weeks and 16weeks. At each visit patients were checked for intra-ocular pressure, BCVA, were checked and Fundus photograph, FFA, and OCT were recorded.

ANALYSIS AND DISCUSSION

I. AGE INCIDENCE

S.No	Age – group (Years)	No of patients	Percentage
1.	50 – 54	—	—
2.	55 – 60	13	26 %
3.	61 – 70	21	42 %
4.	71 – 80	14	28 %
5.	81 – 90	2	4 %

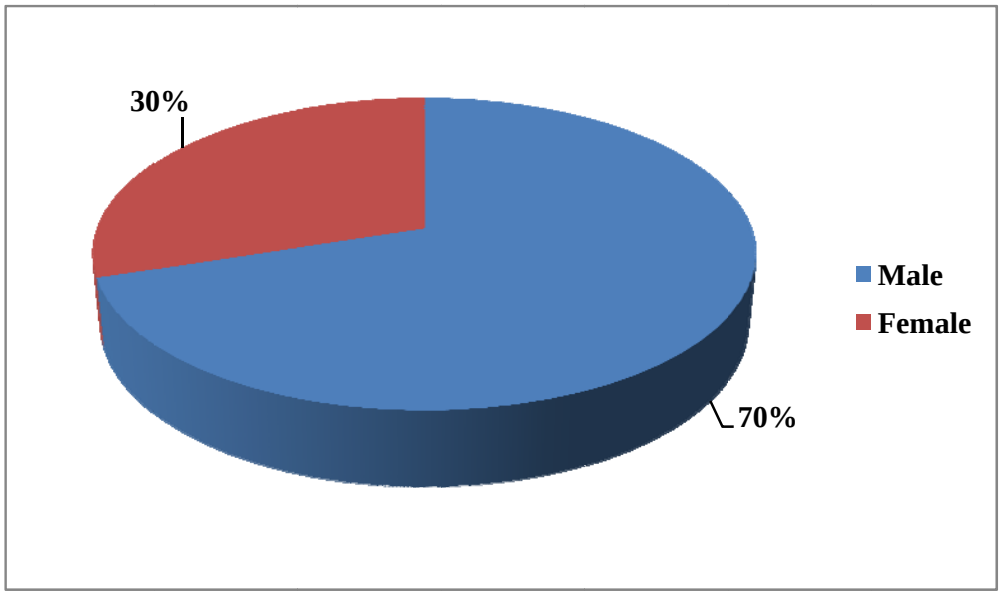


In our study the predominant age group to be afflicted is the 61 – 70 year range followed by 71- 80 year range followed by 55 – 60 year range, two patient between the age of 81 – 90 years were affected. This low incidence could be explained by the decreased life span of people in our country. None of our patients were below the age of 55 years.

This finding correlates with the study in western countries.

II. SEX INCIDENCE

Sex	No of patients	Percentage
Male	35	70 %
Female	15	30%

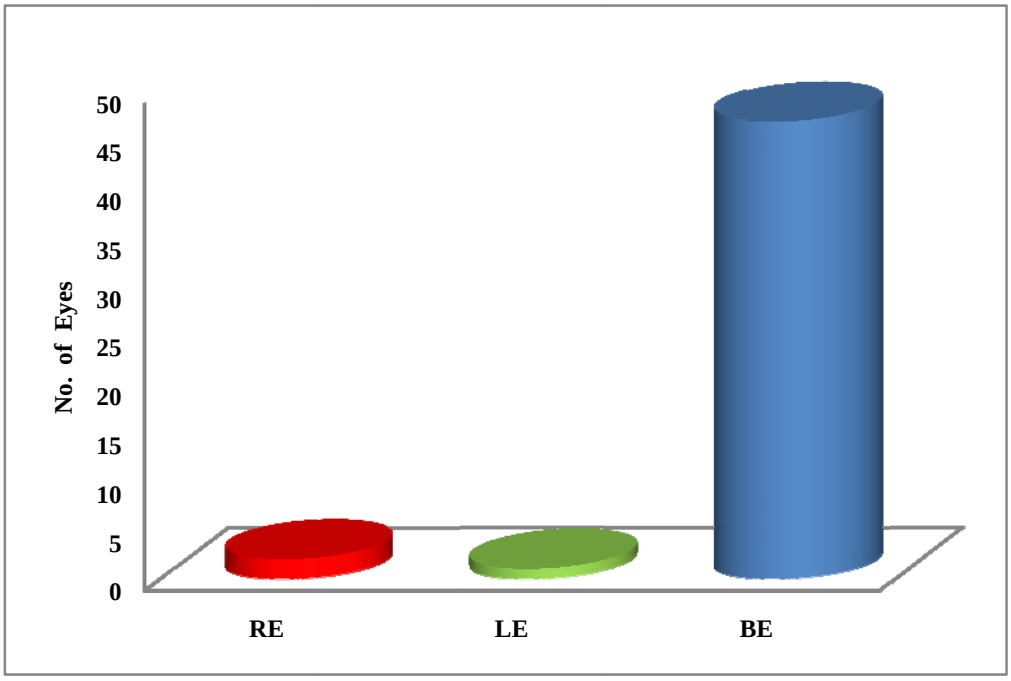


The ratio of males to females in our study was 2.3 : 1. The predominant age group in which males and females were affected was between 61 – 70 years.

In the Framingham Eye study females outnumbered males. Another study by Hanes showed women to have equal prevalence as men. The lower prevalence rate in women in our study could probably be explained by the fact that in our country, females are usually housewives. They are not aware of their diminished vision as they do not do fine jobs which require good vision. .

III. LATERALITY

	Right Eye only	Left Eye only	Both Eyes
Number	2	1	47
Percentage	4%	2%	94%

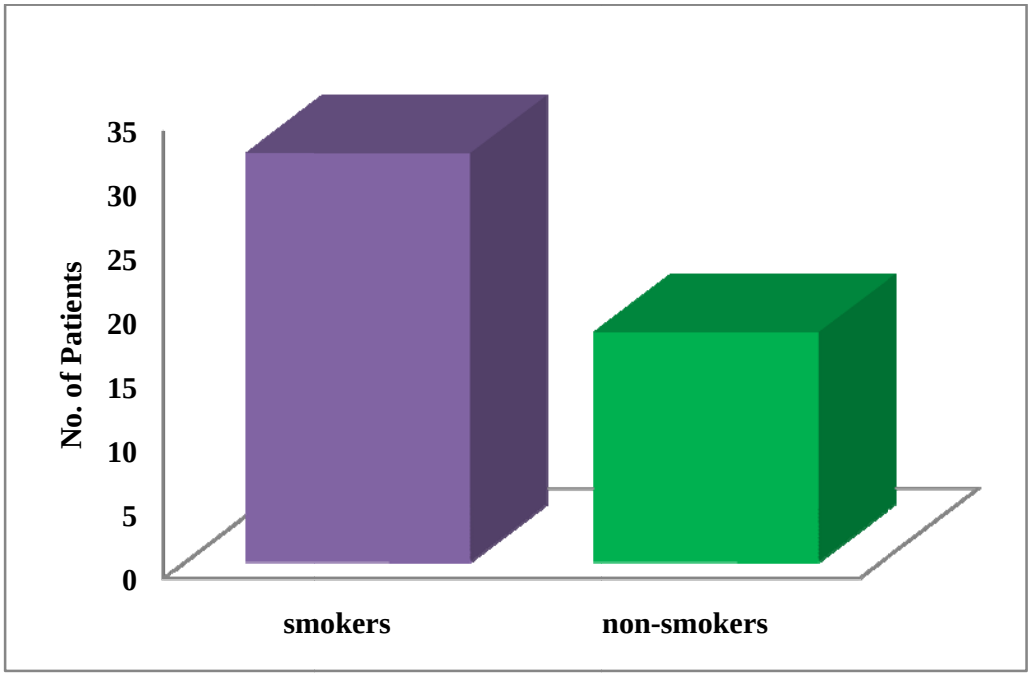


In our study 94% of the patients had bilateral involvement. Among the 3patients who presented with unilateral involvement, 2 patients had RE involvement and 1patient had LE involvement.

This exemplifies the fact that AMD is a bilateral, although assymetrically affecting both eyes.

IV. PERSONAL HABITS

Total no of patients -50	No of patients	Percentage
Smokers	32	64%
Non smokers	18	36%

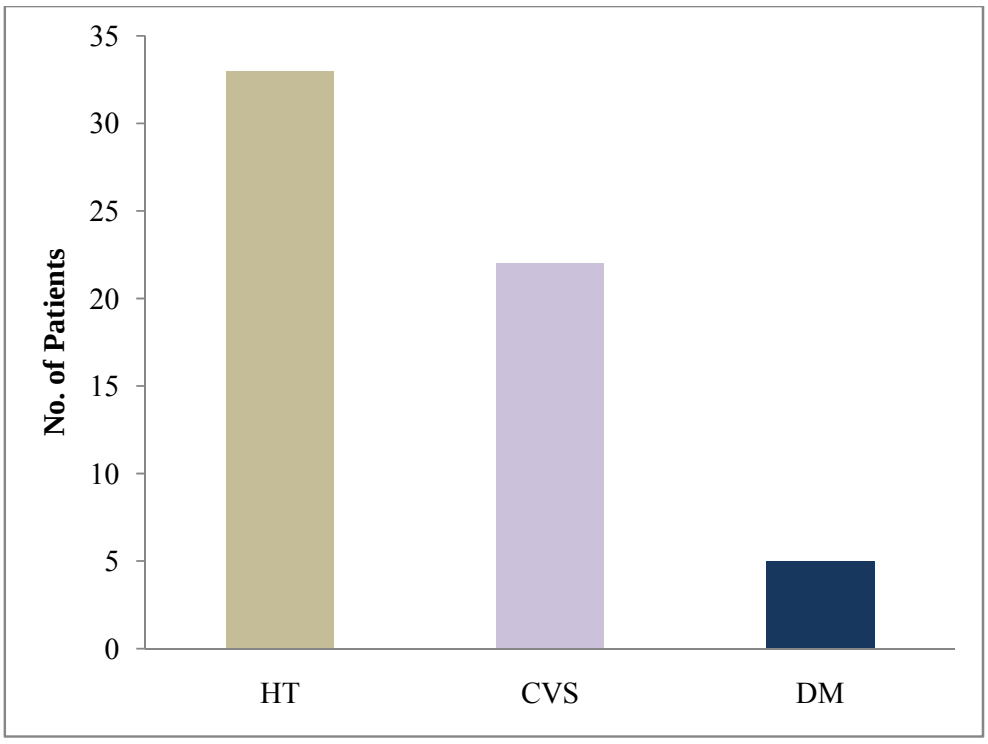


In our study 64% of the patients were chronic smokers. According to Stephen Ryan a definite association exists between AMD and cigarette smoking [6].

This correlation needs elaborate study to explain the pathophysiology of the affection.

V. HIGH RISK FACTORS

Total no of patients- 50	No of patients	Percentage
Hypertension	33	66 %
Cardiac ailments	22	44 %
Diabetes	5	10 %



In our study 66% of the patients who were afflicted with AMD had hypertension.

According to Stephen Ryan, conflicting results have appeared for the association between hypertension and AMD[6].

44% of the patients in our study had non specific cardiac ailments. Most of the patients had non specific angina. So cardiologist opinion was obtained for all the cardiac patients before giving avastin injection.

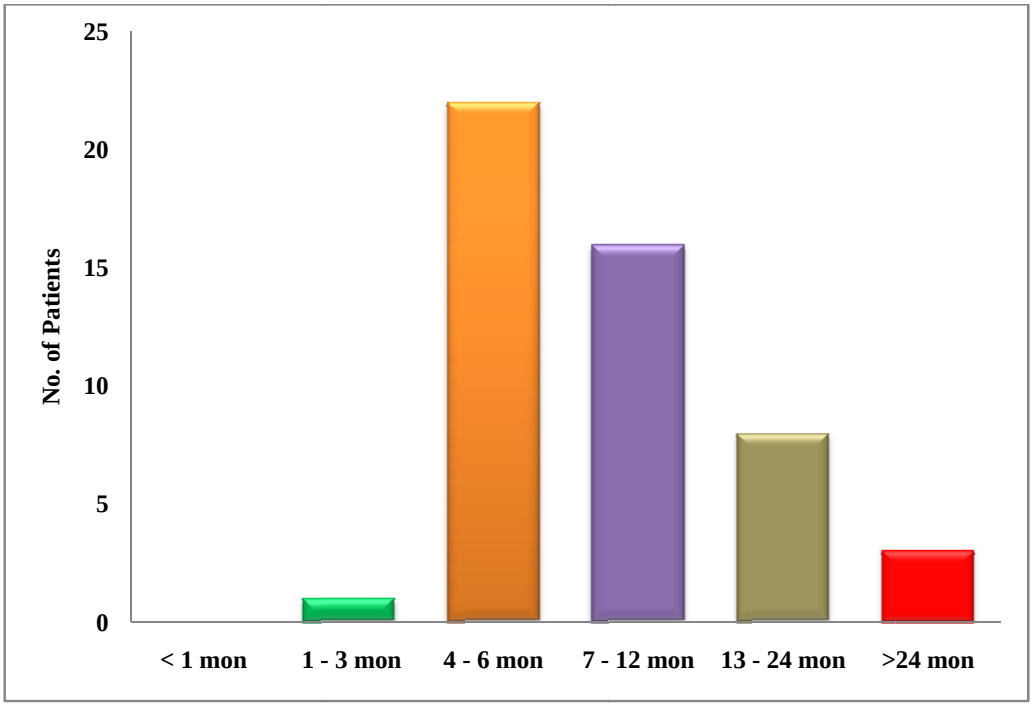
According to Ryan a definite association seems to exist between AMD and cardiovascular disease[6].

This study also correlates with the finding of Stephen Ryan.

Five patients in our series had diabetes mellitus.

VI . DURATION OF DEFECTIVE VISION

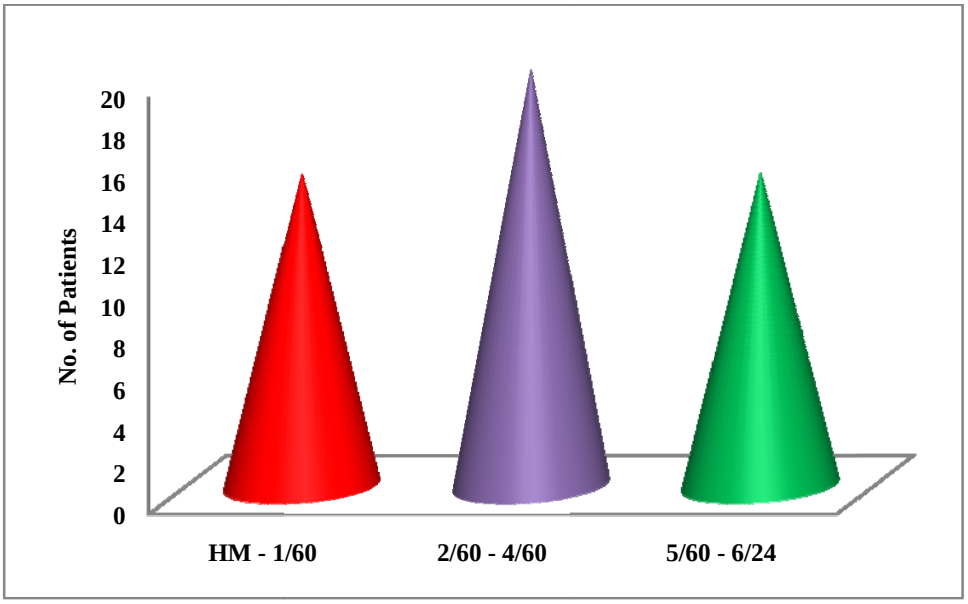
Sl.No.	Duration of Defective vision	Total No	Percentage
1.	Less than one month	Nil	Nil
2.	1 month - 3 months	1	2%
3.	4 months - 6 months	22	44%
4.	7 months - 12 months	16	32%
5.	13 months - 24 months	8	16%
6.	More than 24 months	3	6%



In our study most of the patients reported to the hospital very late in the course of the disease. 44% of the patients reported between 4 months-6 months and 32% between 7-12 months. Only 2% of the patients reported less than 3 months after symptoms appeared.

VII . VISUAL ACUITY ON PRESENTATION

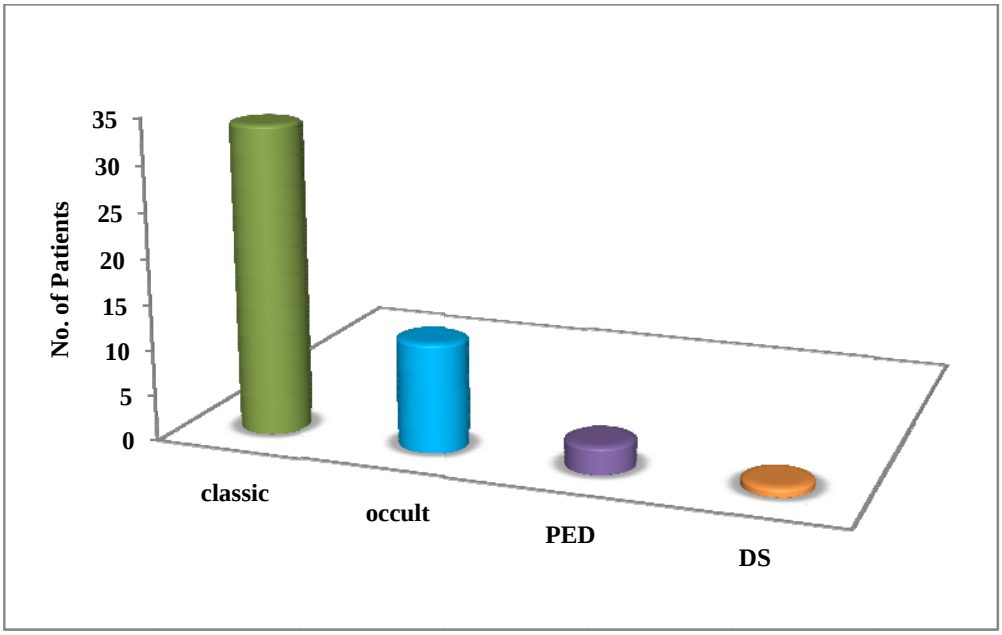
Vision	No of patients	Percentage
HM – 1 / 60	15	30 %
2 / 60 – 4 / 60	20	40 %
5 / 60 – 6 / 24	15	30 %



In our series 30% of the patients presented to us very late in the course of the disease, when the vision was less than 1/60. 40% of patients presented when the VA was 2/60 – 4/60 and 30% between 6/60 and 4/60.

VIII. FLUORESCEIN ANGIOGRAPHY FINDINGS

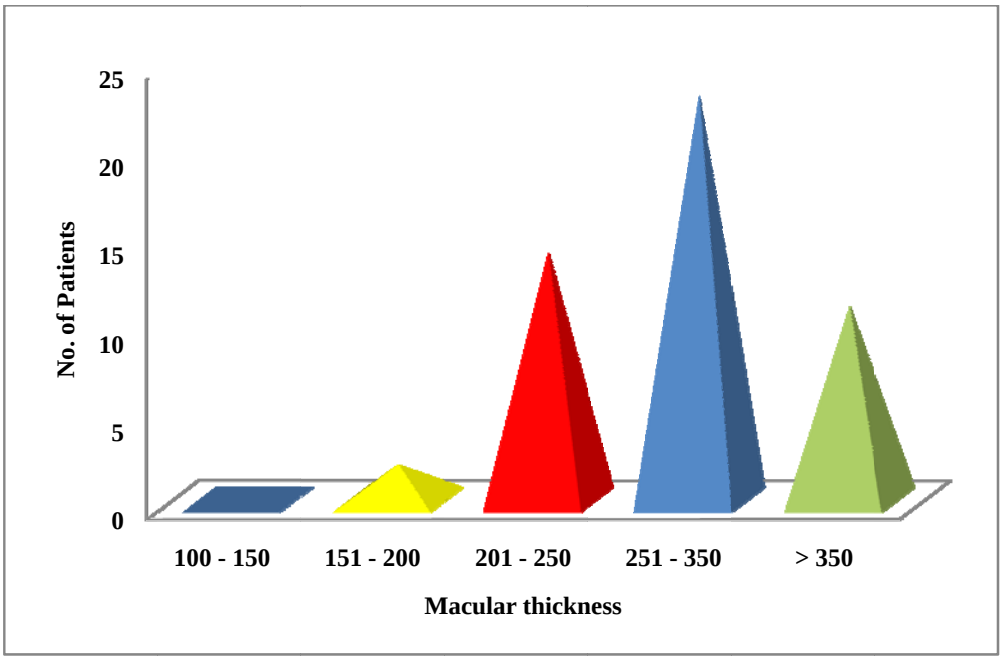
Types	No of patients	Percentage
Classic CNVM	34	68 %
Occult CNVM	12	24 %
PED	3	6 %
Disciform scar	1	2 %



In our study 68% of patients were with classical angiographic type with CNV, 24 % patients were occult type, 6 % of patients were PED and 2 % patients were disciform scar type.

IX. OPTICAL COHERENCE TOMOGRAM

MACULAR THICKNESS	NO OF CASES	PERCENTAGE
100 – 150µ	0	0
151 – 200µ	2	4 %
201 – 250µ	14	28 %
251 – 350µ	23	46 %
➢ 350µ	11	22 %



About 46% of patients were with macular thickness between 250 - 350µ and 22% of patients were with thickness more than 350µ and there were no patients with macular thickness less than 150µ.

X. MEDICAL MANAGEMENT

Injection Bevacizumab (Avastin)

A commercially available bevacizumab (1.25mg/0.05ml) was prepared for each patient and placed in a tuberculin syringe using aseptic techniques. After the eye had been prepared in a standard fashion using 5% povidone iodine and topical antibiotics, 1.25 mg (0.05 ml) of bevacizumab was injected intravitreally via the parsplana 3mm from limbus in aphakia, 3.5mm from limbus in pseudophakia, 4mm from limbus in phakic patient in inferotemporal quadrent. After the injection, intraocular pressure and retinal artery perfusion were checked, and patients were instructed to administer topical antibiotics for 3 days. Patients were called 3 days after injection and were re examined within 1 week.

Patients received reinjections on a monthly basis until pigment epithelial detachment (PED) / or neovascularization resolved.

MAIN OUTCOME MEASURES

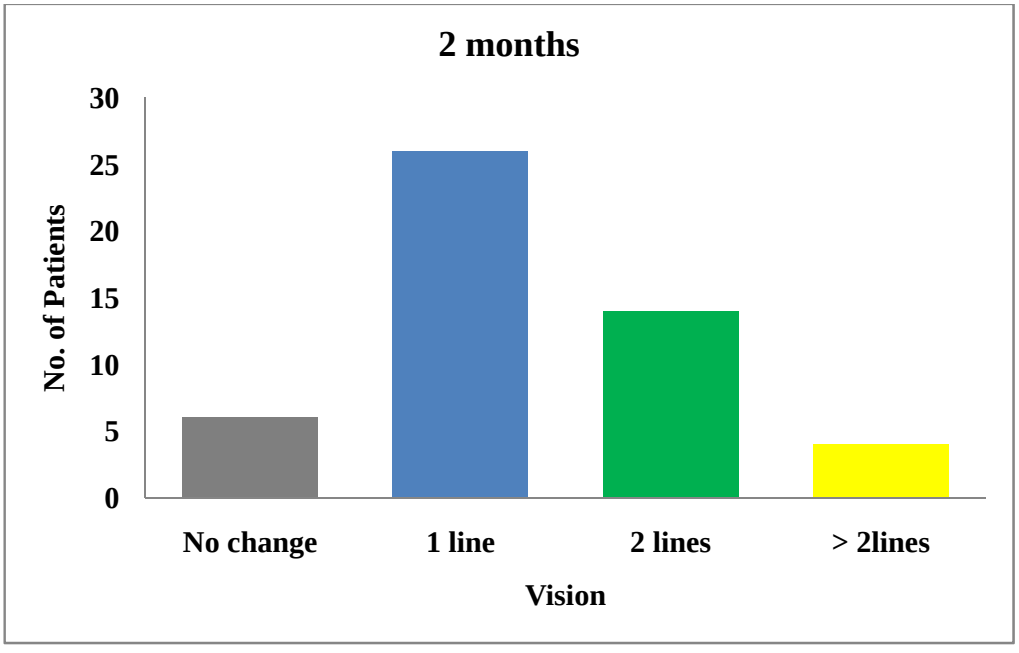
* Best corrected visual acuity (Snellen's chart)

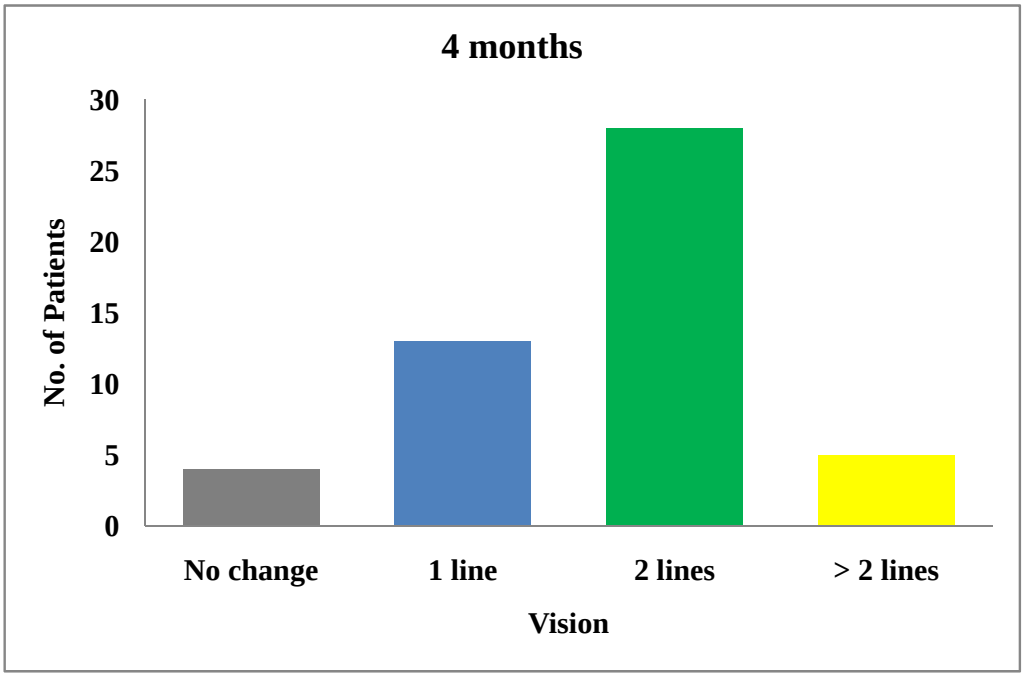
* Macular thickness by OCT (SPECTRAL)

* Changes in Fluorescein angiogram patterns in the form of reduction in size of the lesion and decrease in leakage.

IMPROVEMENT IN VISUAL ACUITY

Lines of improvement	At 2 months	At 4 months
No change	6	4
1 line	26	13
2 lines	14	28
➢ 2 lines	4	5

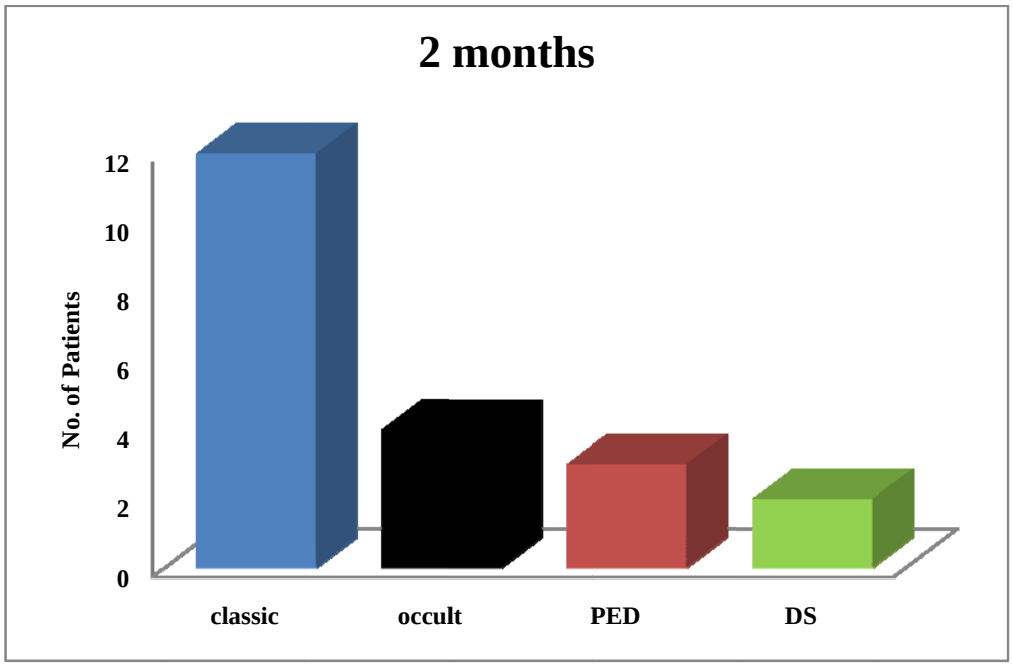


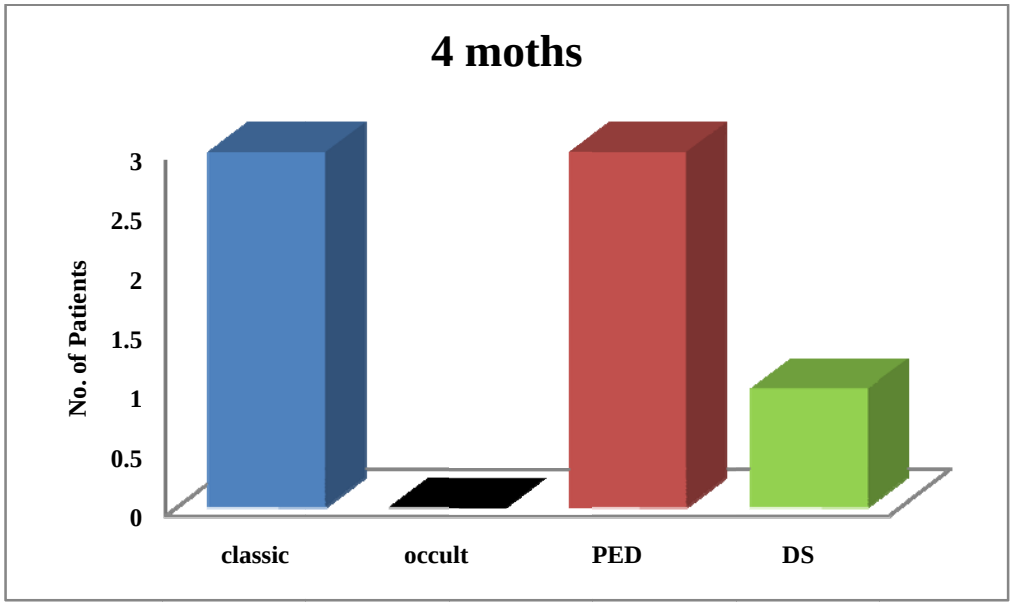


Most of the cases showed no change in visual acuity in 2 weeks, but about 52% cases with classic CNV showed 1 line improvement at the end of 2 months and 56% of cases showing 2lines improvement at the end of 4 months which correlates with Rich RM, Rosenfeld – et-all Retina ; 26:495-511. 8% patient showed no improvement at the end of 4 months. 50% of occult CNV showed more than 2 line improvement at 4 months which is in par with Geitzenauer W – et-all, Klin Monatsbl Augenheilkd 2006; 223:822-7.

ANGIOGRAPHIC PATTERNS

No of cases with leakage	At 2 months	At 4 months
Classic CNVM	12	3
Occult CNVM	4	–
PED	3	3
Disciform scar	1	1

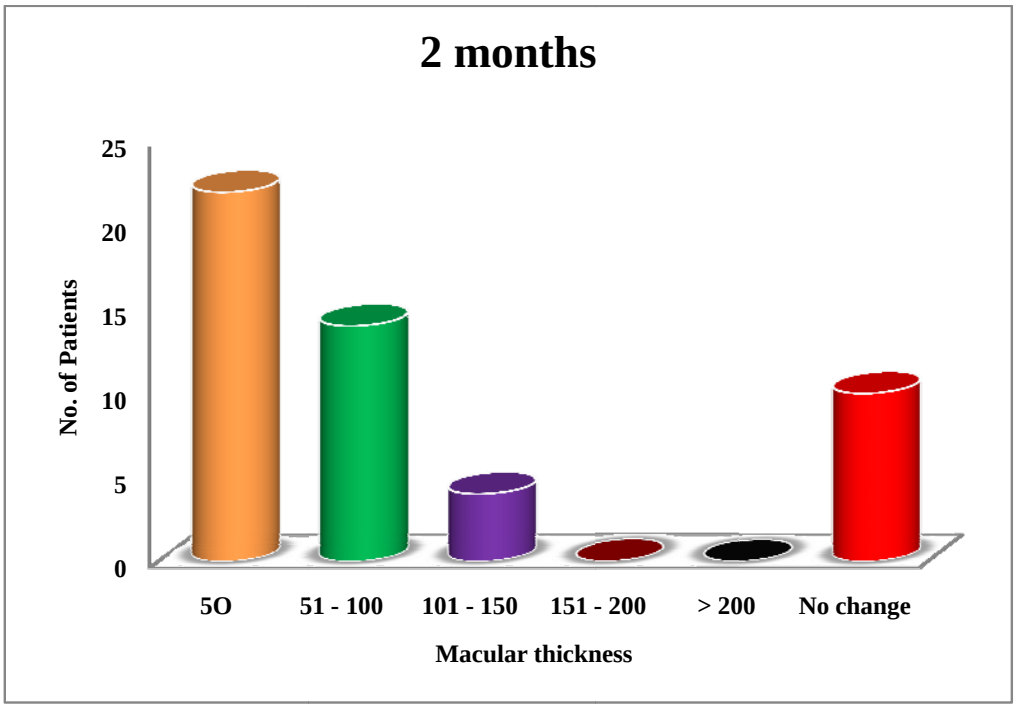


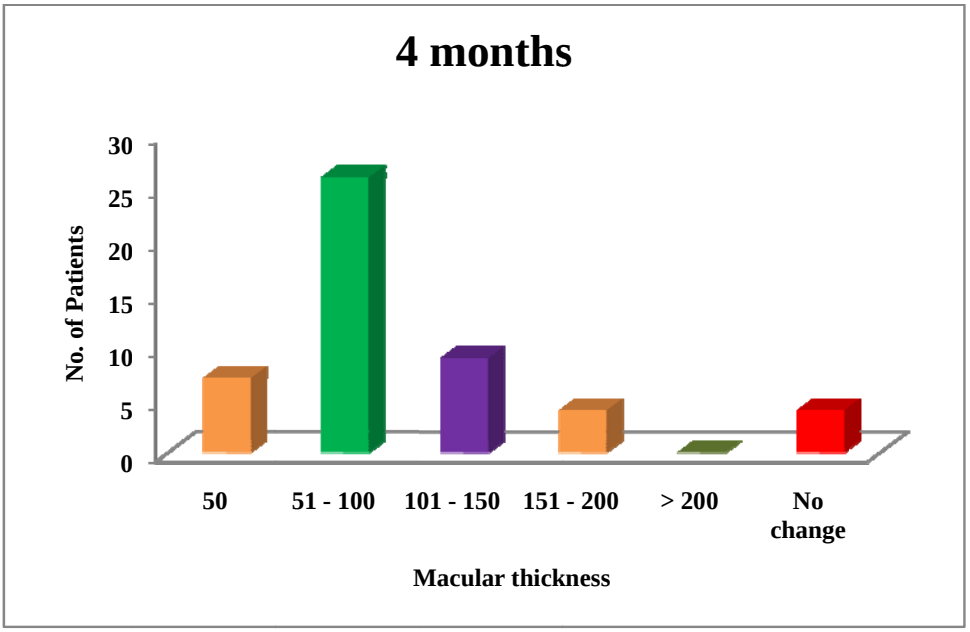


At the end of 4 weeks, 50% of both occult and classic types showed leakage and at the end of 4 months no cases of occult CNV showed leakage which supports the study of Aiesenbrey et-all Graefes Arch Clin Exp Ophthalmol 2007; 245:941-8. 1 patient FFA shows leakage with staining at the end of 4 months because of macular scarring.

REDUCTION IN MACULAR THICKNESS

Reduction in macular thickness	At 2 months	At 4 months
Upto 50	22	10
51 – 100	14	17
101 - 150	4	11
151 - 200	–	5
➢ 200	–	–
No change	10	7





About 50% of Classic CNV and 40% of Occult CNV showed reduction in macular thickness of 50µ at the end of 2month, and 52% of both CNV types showed reduction of 100µ at the end of 4months which correlates well with the study of Moschos MM – et-all Doc Ophthalmol 2007; 114:37-44. 2% patient showed no improvement and he was found to have CNVM with scar formation.

SUMMARY

TO SUMUP IN THE STUDY

1. 50 patients were studied during June – 2008 to November – 2009

2. Of these 50 patients studied, 37 patients were above the age of 60 years and the remaining 13 patients were below 60 years.

3. The ratio of males to females in our study is 2.3 : 1.

4. In our study 94% of the patients had bilateral involvement although both eyes were afflicted asymmetrically

5. More than 60% of the patients were chronic smokers in our series.

6. 66% of the patients had hypertension

7 . More than 44% of the patients in our study had non specific cardiac ailments. Most of the patients had angina, a few patients had previous history of myocardial infarction.

8. In our study most of the patients reported to the hospital very late in the course of the disease. 44% of the patients reported between 4 months-6 months and 32% between 7-12 months.

9. In our series 30% of the patients presented to us very late in the course of the disease, when the vision was less than 1/60. 41% of

patients presented when the VA was 2/60 – 4/60 and 29% between 6/60 and 4/60.

10. In our study 68% of patients were with classical angiographic type with CNV, 24 % patients were occult type, 6 % of patients were PED and 2 % patients were disciform scar type.

11. About 46% of patients were with macular thickness between 250 - 350µ and 22% of patients were with thickness more than 350µ and there were no patients with macular thickness less than 150µ.

12. All the patients were given 1.25mg of Bevacizumab intravitreally under aseptic precautions after explaining the procedure who then signed a consent form. Follow-up ranged from 2 to 16 weeks. All 50 patients completed a 16-week follow-up visit.

13. During each follow-up, patients were checked for improvement in V/A, decrease in macular thickness and change in angiographic patterns. Fundus photographs were taken for documentation.

14. 52% cases with classic CNV showed 1 line improvement in snellen's chart at the end of 2 months and 56% of cases showing 2 lines improvement at the end of 4 months.

15. At the end of 2 months 24% of CNV showed leakage in the fluorescein angiography and 5% of leakage in 4 months

16. The qualitative assessment of the OCT showed marked reduction in subretinal fluid and cystic oedema 1month after injection. The earliest sign of reduction was the disappearance of SRF. About 50% of Classic CNV and 40% of Occult CNV showed reduction in macular thickness of 50μ at the end of 2 months, and 52% of both CNV types showed reduction of 100μ at the end of 4months.

CONCLUSION

The following conclusions were arrived at from the above study.

1. The incidence of AMD is high above the age of 60 years. This correlates with the Framingham Eye study.

2. The sex incidence in our study reveal that males are more affected than females (ratio 2.3:1). This does not correlate with the existing studies. This may be explained by the fact that in our society most of the skilled jobs are being carried out by males. Since most of the female patients are housewives they are not aware of the deterioration in vision and are not reporting to the hospital.

3. 94% have bilateral although asymetrical involvement of eyes.

4. The Amsler Grid chart is one of the useful diagnostic test for follow up.

5. 60% of the patients were chronic smokers in our series. In this regard there is scope for further detailed study in correlating the precipitating factor for AMD.

6. Hypertension (66%) and cardiovascular disease (44%) are found to be the common systemic diseases associated with AMD.

7. FFA is very useful diagnostic tool in classifying the type of AMD and also to decide on the treatment modality.

8. OCT is useful in follow-up period.

9. After inj Avastin 52% cases with classic CNV showed 1 line improvement in snellen's chart at the end of 2 months and 56% of cases showing 2 lines improvement at the end of 4 months which correlates with Rich RM, Rosenfeld – et-all Retina ; 26:495-511

10. At the end of 4 weeks, 50% of both occult and classic types showed leakage and at the end of 4 months no cases of occult CNV showed leakage which supports the study of Aiesenbrey et-all Graefes Arch Clin Exp Ophthalmol 2007; 245:941-8.

11. About 50% of Classic CNV and 40% of Occult CNV showed reduction in macular thickness of 50µ at the end of 2 months, and 52% of both CNV types showed reduction of 100µ at the end of 4months ,which correlates well with the study of Moschos MM – et-all Doc Ophthalmol 2007; 114:37-44.

12. Followup period of the patients ranged from 3 months to 8 months. Very few patient was reported for regular followup. Reasons for this could be due to the old age patients were finding it difficult for a regular visit to hospital

In India ophthalmologists feel that AMD is an uncommon condition. By this study we prove that although its prevalence rate is low in India compared to western countries, Indians are not immune from developing AMD.

In conclusion, I would like to add that there still exists grey areas in the understanding of AMD like its possible etiology, an effective medical treatment, as well as the effect of laser photo coagulation. The vast array of work done throughout the world regarding these aspects in AMD, amply testifies to the fact that the last word with regards to this disorder is yet to be written. Before concluding I would like to quote Benjamin Boyd who said

"I cannot think of a more frustrating situation as clinical ophthalmologist than to see our patients deteriorate in sight and spirit as they develop AMD".

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PROFORMA

Name Age Sex Occupation

Op no

Address

Chief complaints:

. Defective vision
. Metamorphopsia
. Floaters

Past history:

. Diabetes- duration treatment
. Hypertension duration treatment
. Cardiovascular disease duration treatment

H/O smoking

Sysetmic examination:

BP PR
RBS Urine-alb & sugar

Cardiovascular system
Ocular examination:

	RE	LE
Visual acuity		
Retinoscopy		
Tension		
Eye lids		
Conjunctiva		
Cornea		
Anterior chamber		

Iris

Pupil

Lens

Fields

Colour vision

Amsler’s grid chart

Fundus examination:

SLE +90D

Indirect ophthalmoscopy

Fundus Fluorescein Angiography

Optical coherence tomography

Injection Bevacizumab (Avastin)

Follow-up

.Visual acuity

.Tension

. Amsler chart

. Fundus by IDO

. FFA

KEY TO MASTER CHART

VA	-	Visual acuity
FFA	-	Fundus Fluorescein Angiography
OCT	-	Optical Coherance Tomogram
HT	-	Hypertension
DM	-	Diabetes
CVS	-	Cardiovascular system
ARMD	–	Age Related Macular Degeneration
SMD	-	Senile Macular Degeneration
FAZ	-	Foveal Avascular Zone
RPE	-	Retinal Pigment Epithelium
BM	-	Bruhs membrane
CNVM	–	Choroidal neovascular membrane
PED	–	Pigment Epithelial Detachment
GA	–	Geographical Atrophy

LIST OF SURGERIES PERFORMED

S. No.	Name	Age	Sex	IP no.	Diagnosis	Surgeries
1.	Gopal	75	M	432578	RE-MC , LE-IMC	RE – ECCE with PCIOL
2.	Devaki	56	F	421634	RE – IMC , LE - NC	LE – ECCE with PCIOL
3.	Narasimman	63	M	431468	RE – MC , LE - MC	RE – ECCE with PCIOL
4.	Kannammal	59	F	443290	BE - NC	RE – ECCE with PCIOL
5.	Pongodi	65	F	479832	RE – MC , LE - IMC	RE – ECCE with PCIOL
6.	Chellappan	81	M	456803	RE – Pseudo , LE - MC	LE – ECCE with PCIOL
7.	Aathi	63	M	409876	RE – MC , LE - IMC	RE – ECCE with PCIOL
8.	Palnisamy	61	M	460983	BE - NC	LE – ECCE with PCIOL
9.	Kasthuri	58	F	456788	RE – PSEUD , LE - MC	LE – ECCE with PCIOL
10.	Meenakshi	64	F	499887	RE – MC , LE -IMC	RE – ECCE with PCIOL
11.	Chitra	35	F	794793	LE - Pterygium	LE – Pterygium excision
12.	Nalliah	67	M	569797	RE- IMC, LE -Pseudo	RE – SICS with PCIOL
13.	Kannan	62	M	637812	RE – Aphakia,LE - MC	LE - ECCE
14.	Revathi	59	F	467901	BE - IMC	RE – SICS with PCIOL

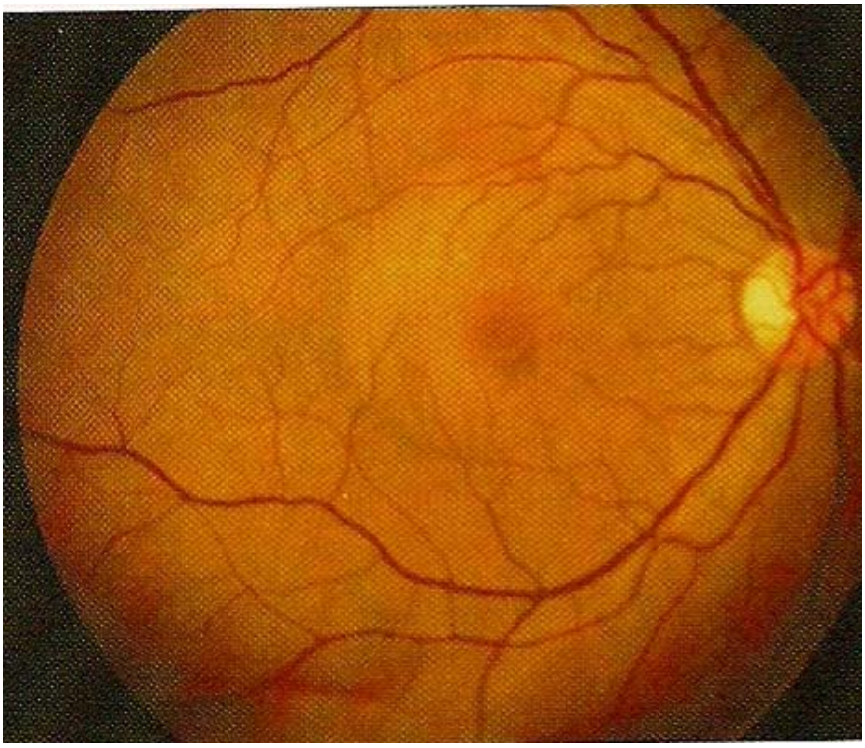
S. No.	Name	Age	Sex	IP no.	Diagnosis	Surgeries
15.	Chinnaponnu	64	F	502167	RE – IMC , LE – NC	LE – SICS with PCIOL
16.	Maran	70	M	50018	RE – Pseudo LE – IMC	LE – SICS with PCIOL
17.	Vasanthakumari	60	F	617917	BE – NC	RE – ECCE with PCIOL
18.	Rajasekar	58	M	483215	RE – IMC LE – MC	LE – SICS with PCIOL
19.	Saroja	74	F	490427	RE – IMC LE - Pseudo	RE – SICS with PCIOL
20.	Dinesh	25	M	47873	LE – Rupture Globe	LE- Corneal sclera tear suturing
21.	Thippu	56	M	78965	RE – MC	RE – SICS with PCIOL
22.	Sabapathy	70	M	86989	RE Panophthalmitis	RE – Evisceration
23.	Gopal	65	M	776441	BE IMC	LE SICS with PCIOL
24	Chandra	65	F	886336	RE -MC LE- Pseudo	RE SICS with PCIOL
25.	Murugan	50	M	85968	LE – Total RD	LE – RD Surgery
26.	Kanniammal	60	F	684392	BE- IMC	LE ECCE with PCIOL
27.	Maragatham	65	F	785391	RE –IMC LE - MC	LE ECCE with PCIOL
28.	Elangovan	76	M	790160	RE- IMC LE- MC	LE ECCE with PI
29.	Perumal	70	M	690437	RE- IMC LE - MC	LE ECCE with PCIOL

S. No.	Name	Age	Sex	IP no.	Diagnosis	Surgeries
30.	Jayagopal	50	M	692899	BE -IMC	RE ECCE with PCIOL
31.	Subramani	57	M	793525	RE- IMC LE - MC	LE ECCE with PCIOL
32.	Kaliammal	68	F	783728	BE- NC	RE ECCE with PCIOL
33.	Annammal	60	F	674267	BE- MC	LE ECCE with PCIOL
34.	Krishnaveni	50	F	725015	BE- IMC	LE SICS with PCIOL
35.	Muniyammal	65	F	816095	BE- IMC	LE SICS with PCIOL
36.	Dhanalakshmi	46	F	785885	BE- IMC	RE SICS with PCIOL
37.	Ramasamy	65	M	826095	BE- IMC	RE SICS with PCIOL
38.	Vasantha	38	F	656005	RE -Pseudo LE -IMC	LE ECCE with PCIOL
39.	Punitha	35	F	75940	RE - Pterygium	RE Autograft/excision
40.	Ravi	64	M	634589	BE - IMC	RE SICS with PCIOL
41.	Vellaiyan	55	M	847637	BE MC	LE ECCE with PCIOL
42.	Dasappan	35	M	87720	LE Exposure keratitis	LE medial tarsorrhaphy
43.	Etiappan	58	M	8912	LE-IMC	LE – SICS withPCIOL
44.	Mariappan	52	M	792726	LE-IMC	LE – SICS with PCIOL

S. No.	Name	Age	Sex	IP no.	Diagnosis	Surgeries
45.	Shanthi	48	F	811986	BE- IMC	RE SICS with PCIOL
46.	Varadhan	46	M	820826	RE- CDC	RE DCR
47.	Sumathy	54	F	762091	LE- CDC	LE DCT
48.	Baskar	52	M	83940	RE-MC LE-IMC	RE – SICS with PCIOL
49.	Venkatesh	56	M	78542	LE-IMC	LE – SICS
50.	Lakshmi	72	F	84286	RE Ch dacryo cystitis	RE - DCT

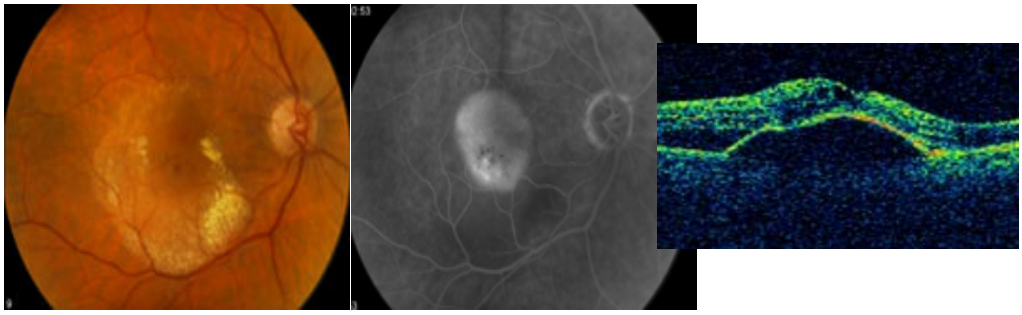
EXUDATIVE ARMD

PED

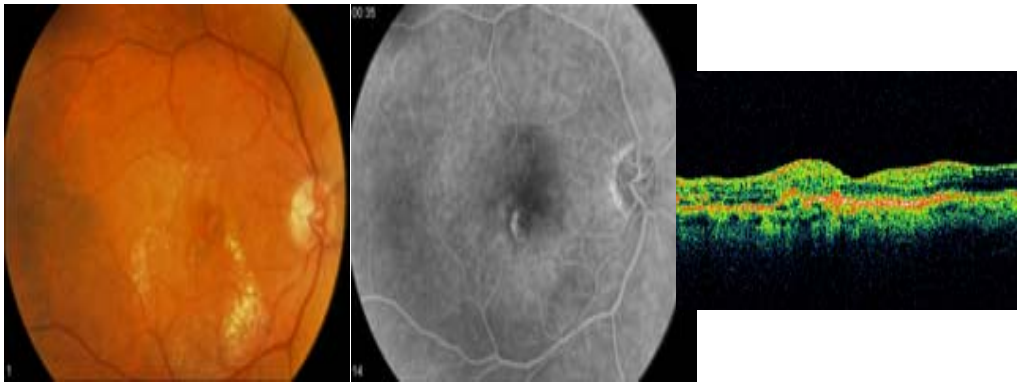


WET AMD WITH MACULAR THICKNESS OF 432µ

PRE-INJECTION



8wks Post-Injection



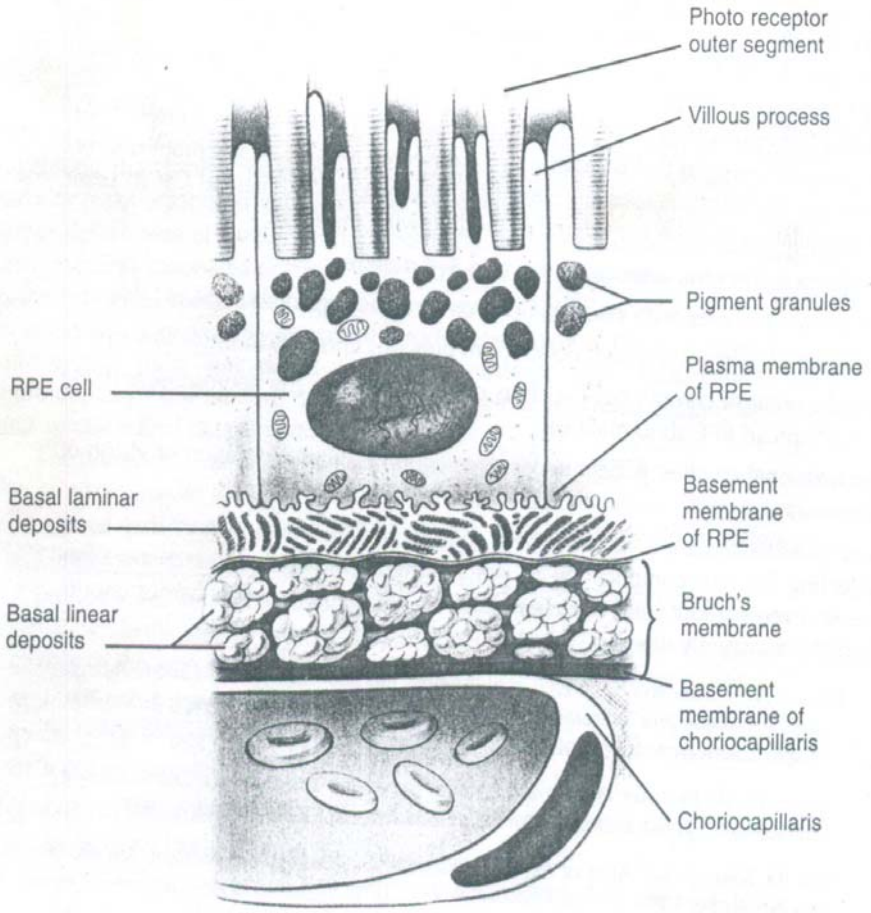
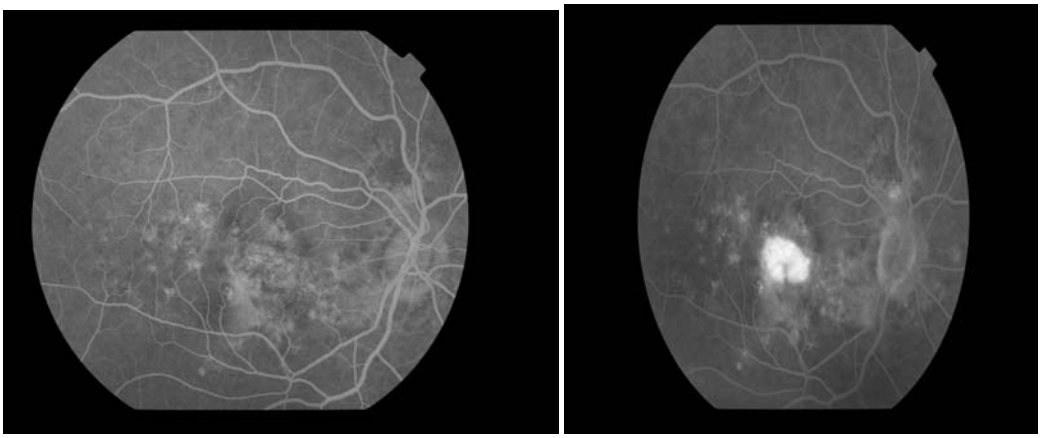
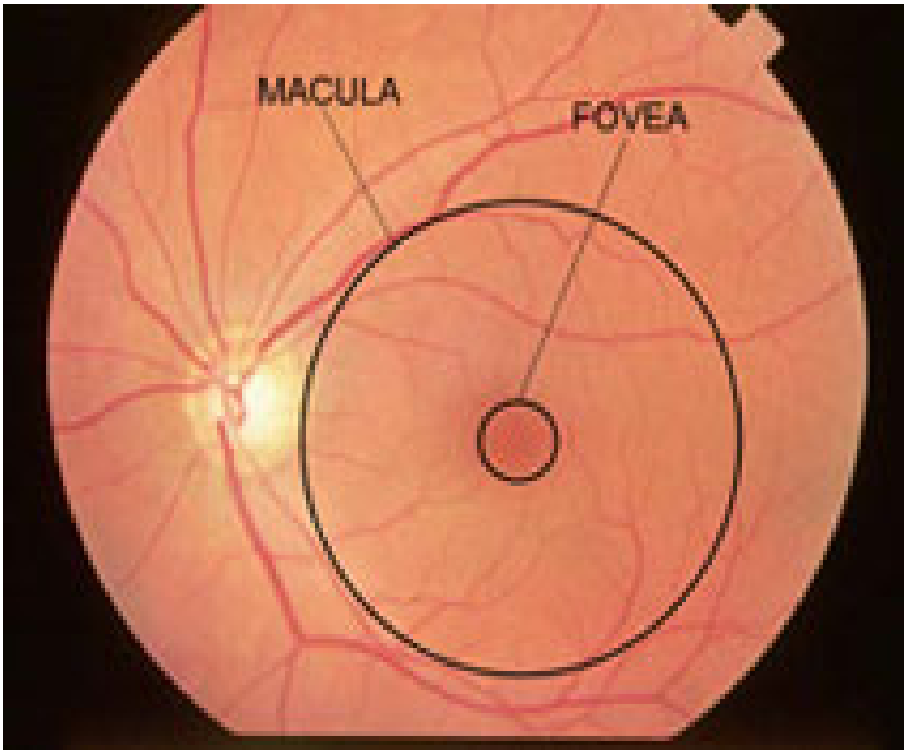


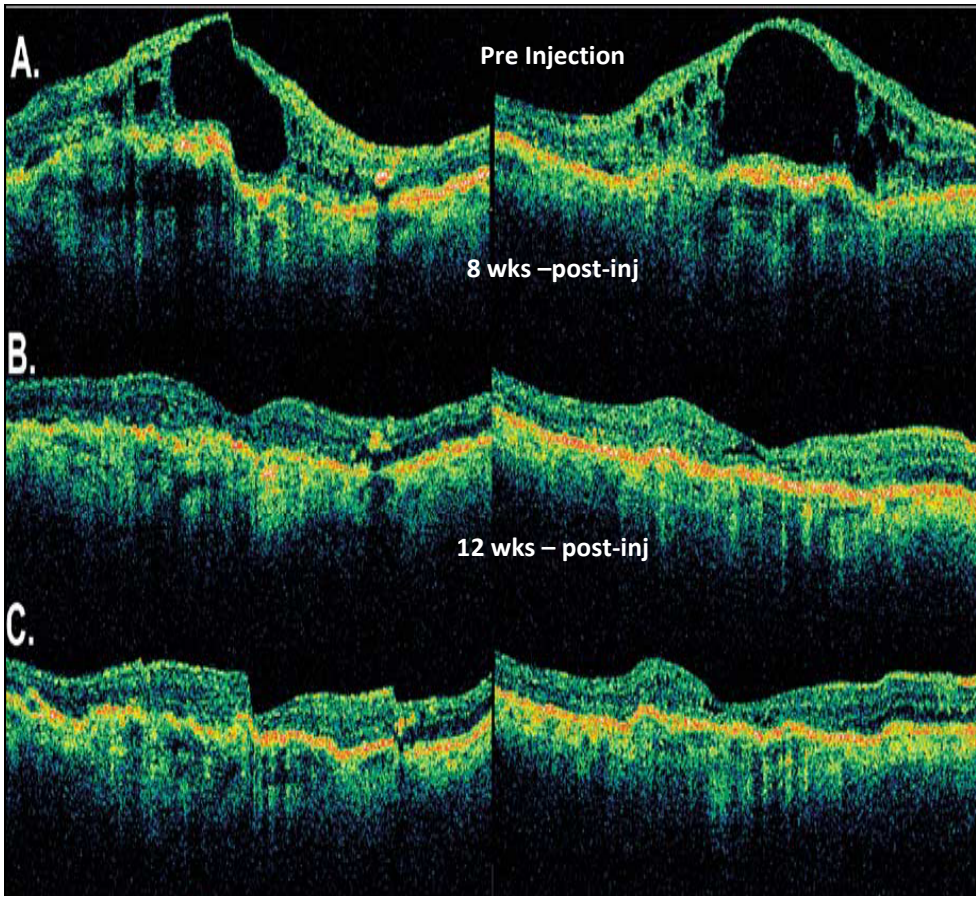
FIG IV-1—Schematic illustration of basal laminar deposits and basal linear deposits that result in a thickened inner aspect of Bruch's membrane. (Illustration by Christine Gralapp.)

DISCIFORM SCAR

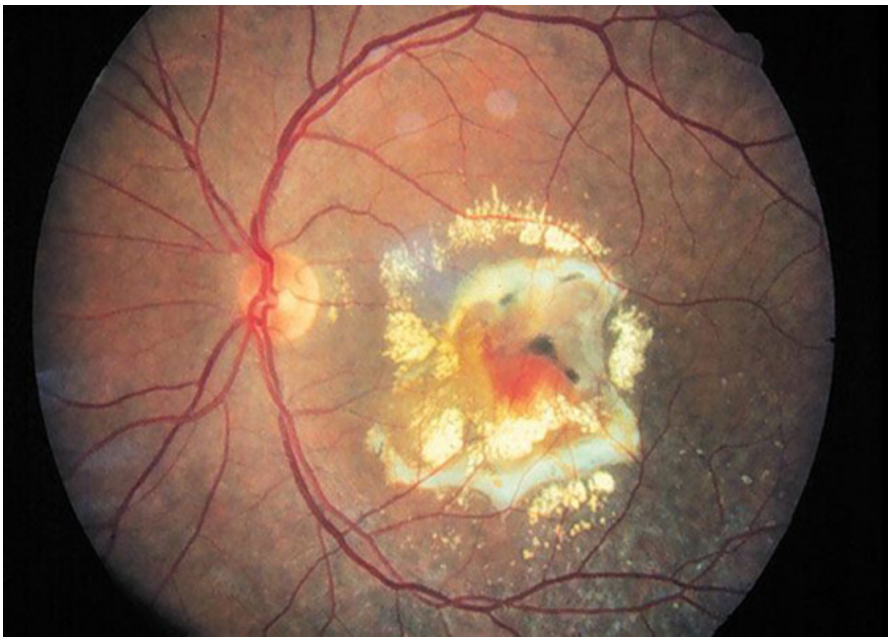


NORMAL FUNDUS



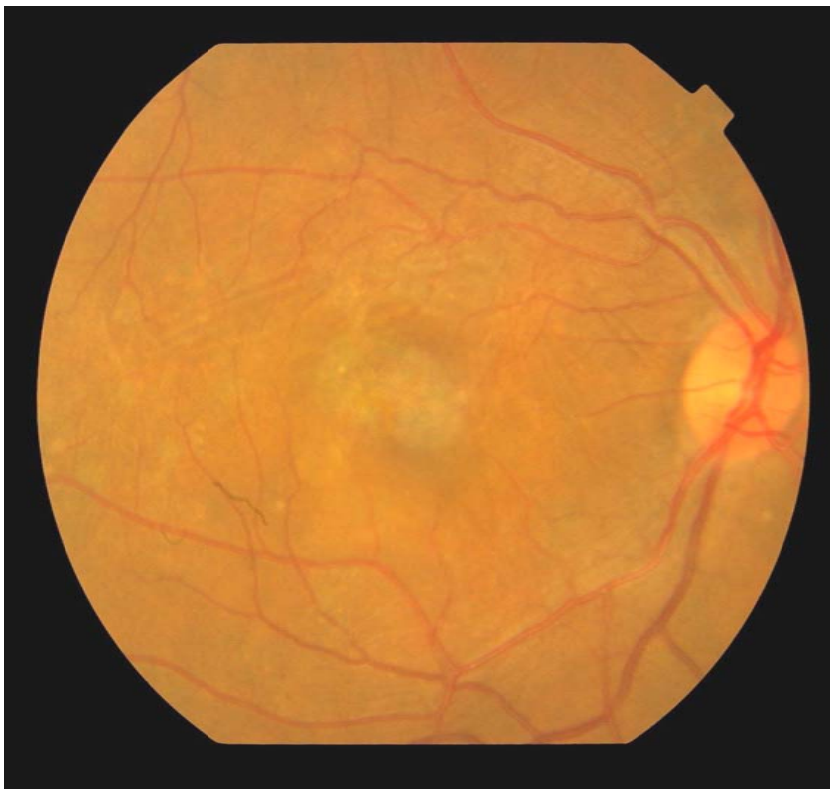

A.
Pre Injection
8 wks –post-inj
B.
12 wks – post-inj
C.

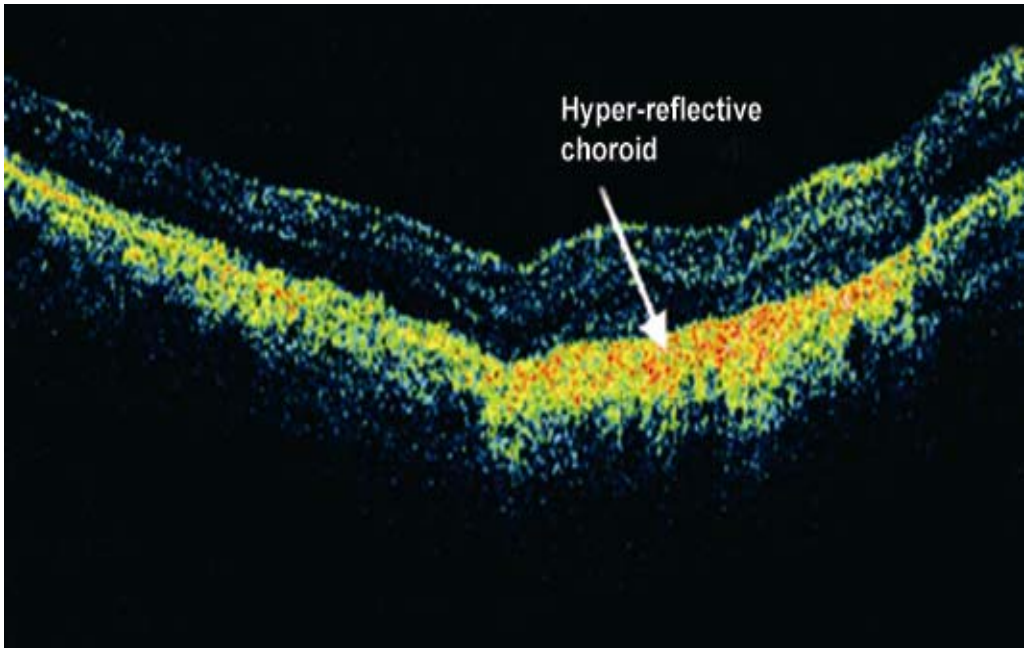
MASSIVE EXUDATION

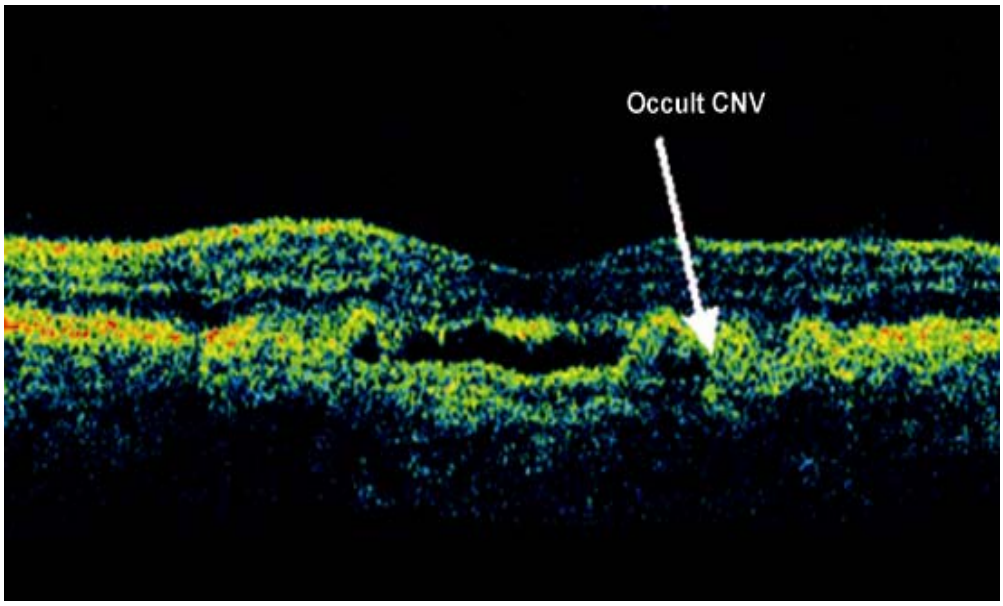


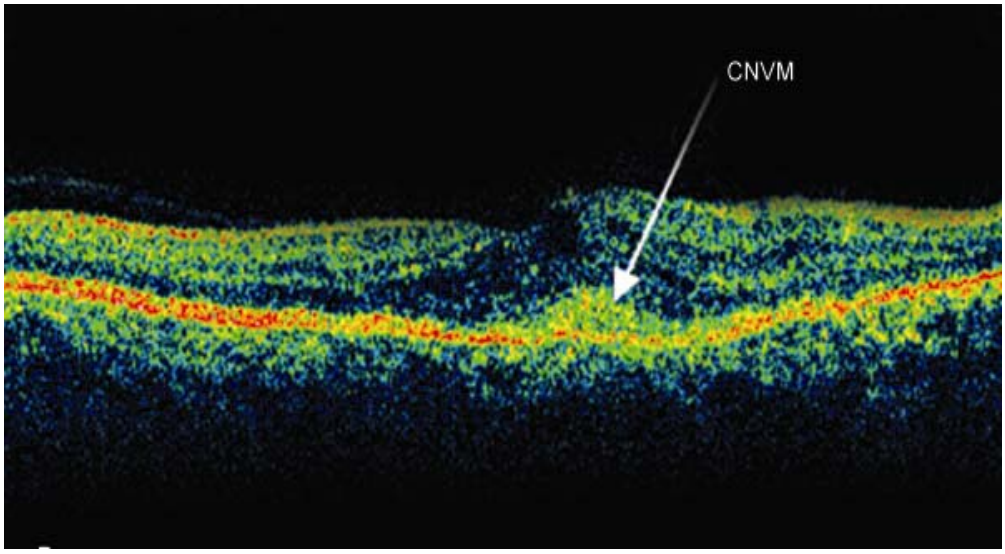
CNVM – VITREOUS HEMORRHAGE

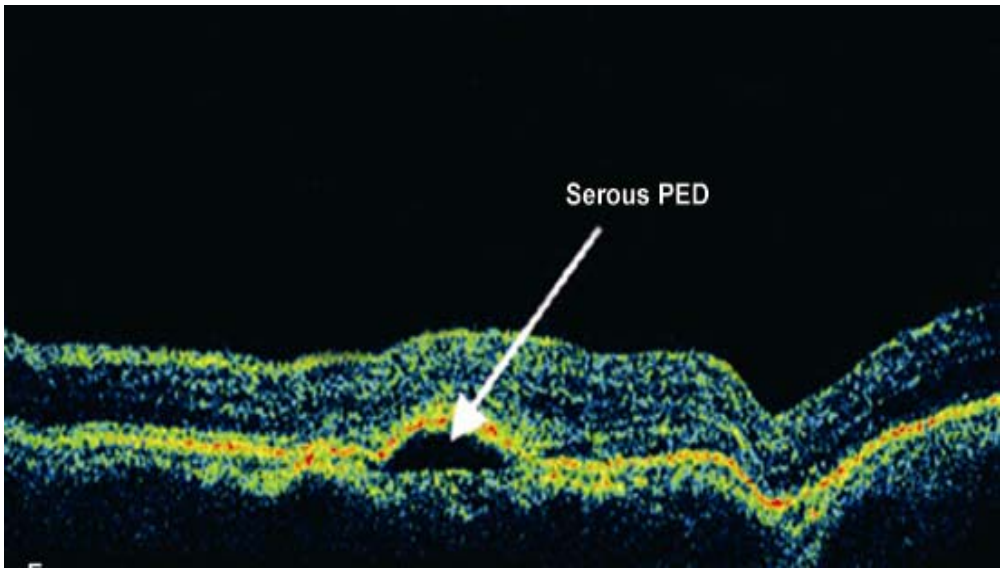
DISCIFORM SCAR

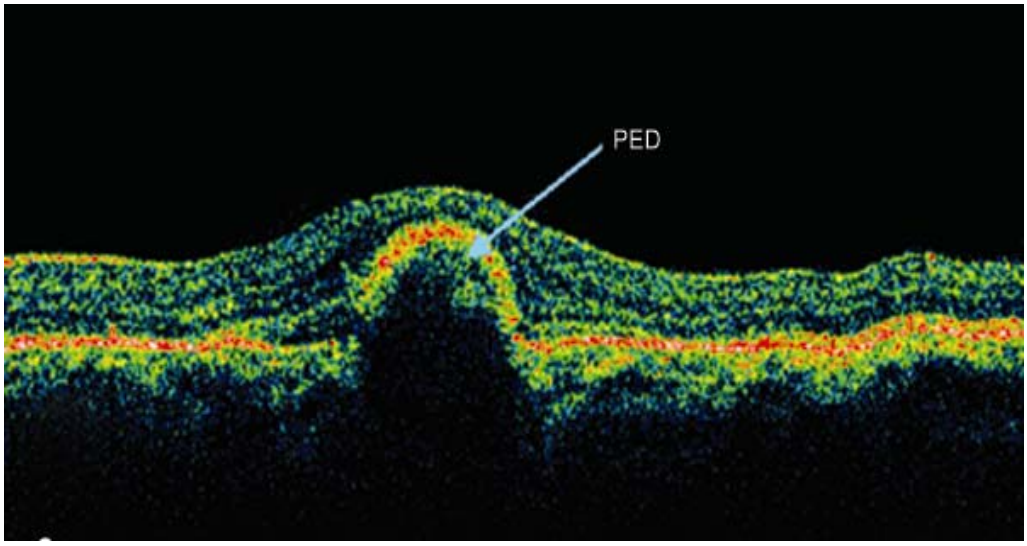



Hyper-reflective
choroid

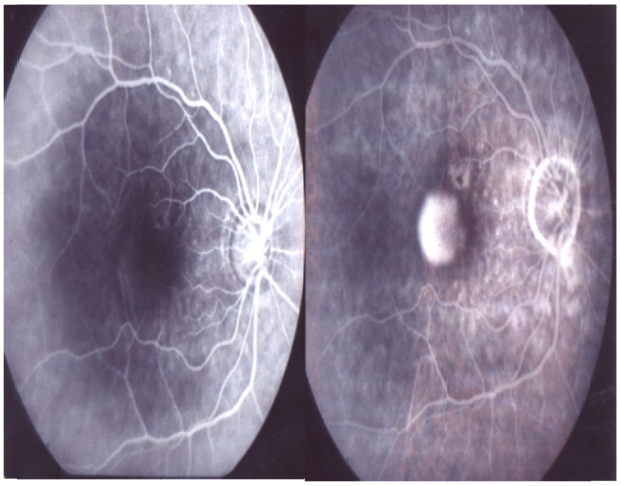

Occult CNV


CNVM


Serous PED

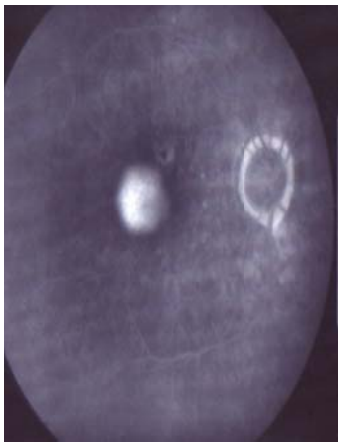

PED

PED



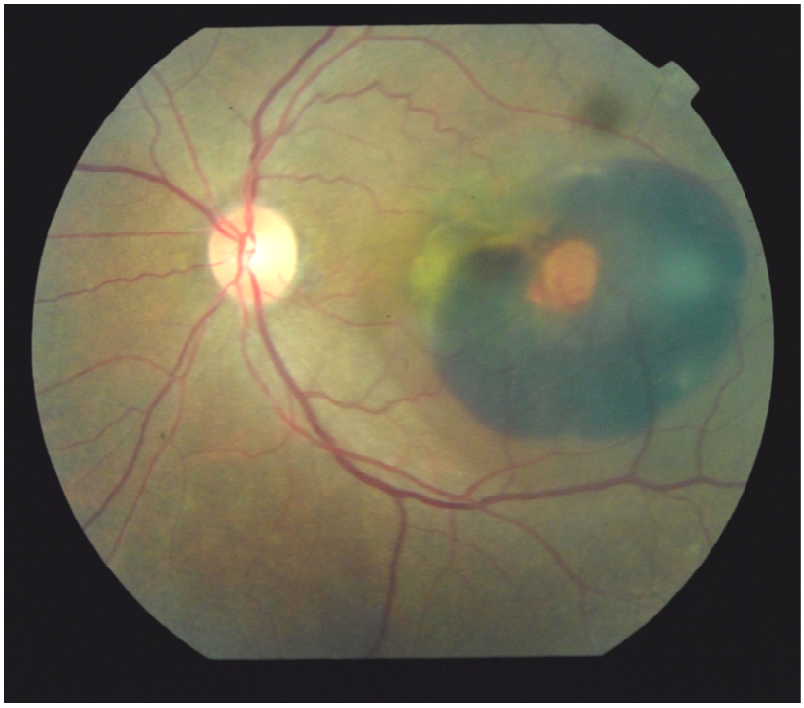
Early, well-defined *hyper*fluorescence

Progressive increase in hyperfluorescence

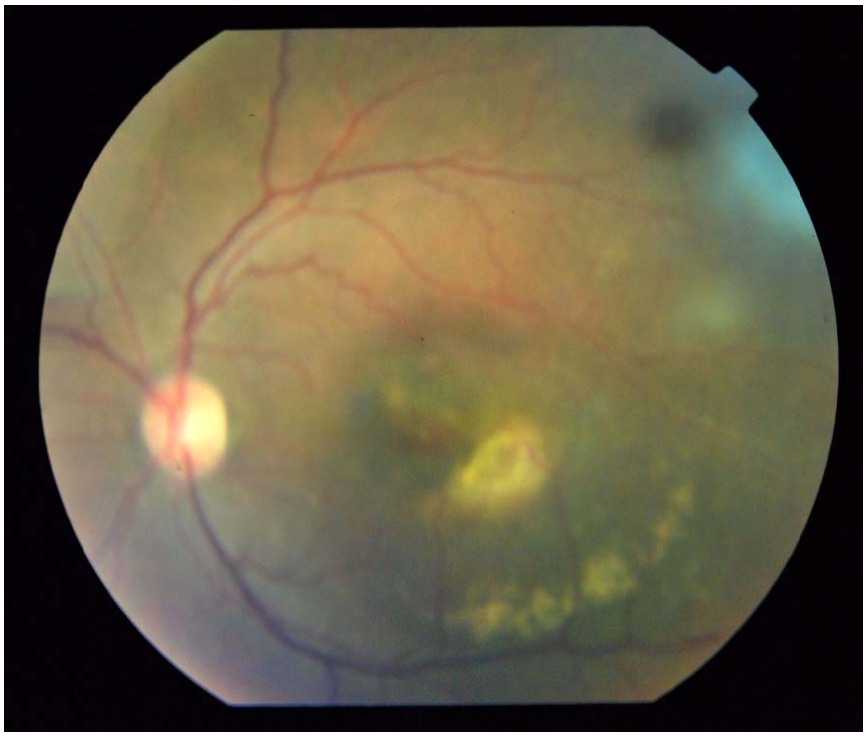


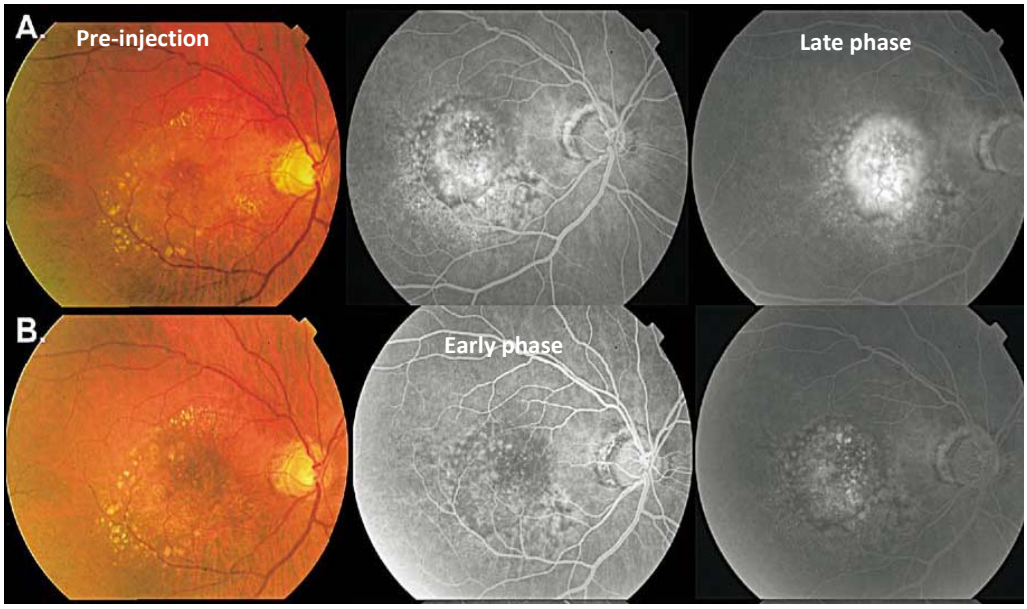
No increase in size of lesion

PRE INJECTION

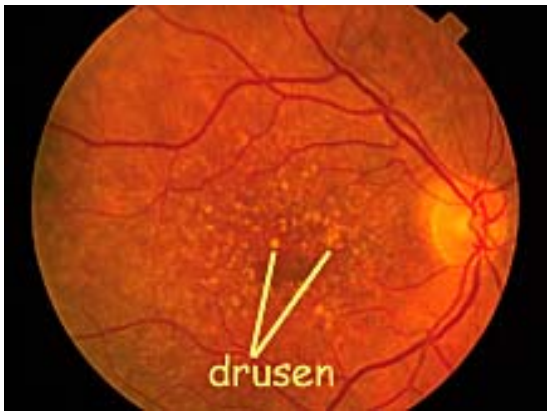


POST INJECTION

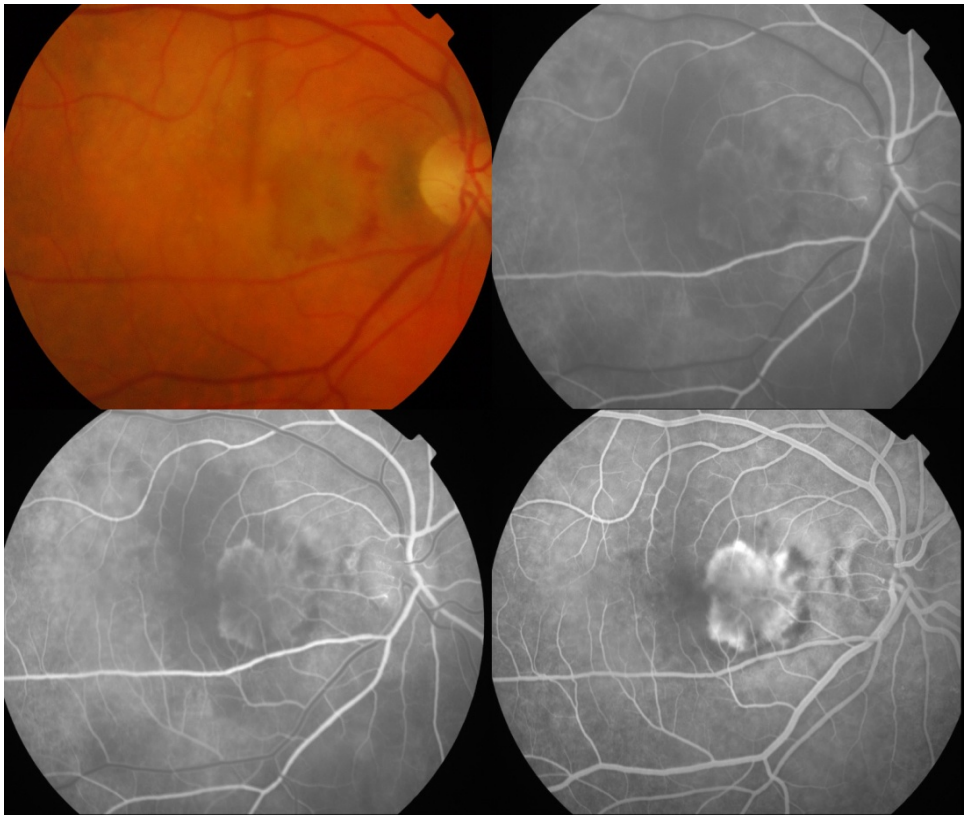



A.
Pre-injection
Late phase
B.
Early phase

DRY ARMD **WET ARMD**



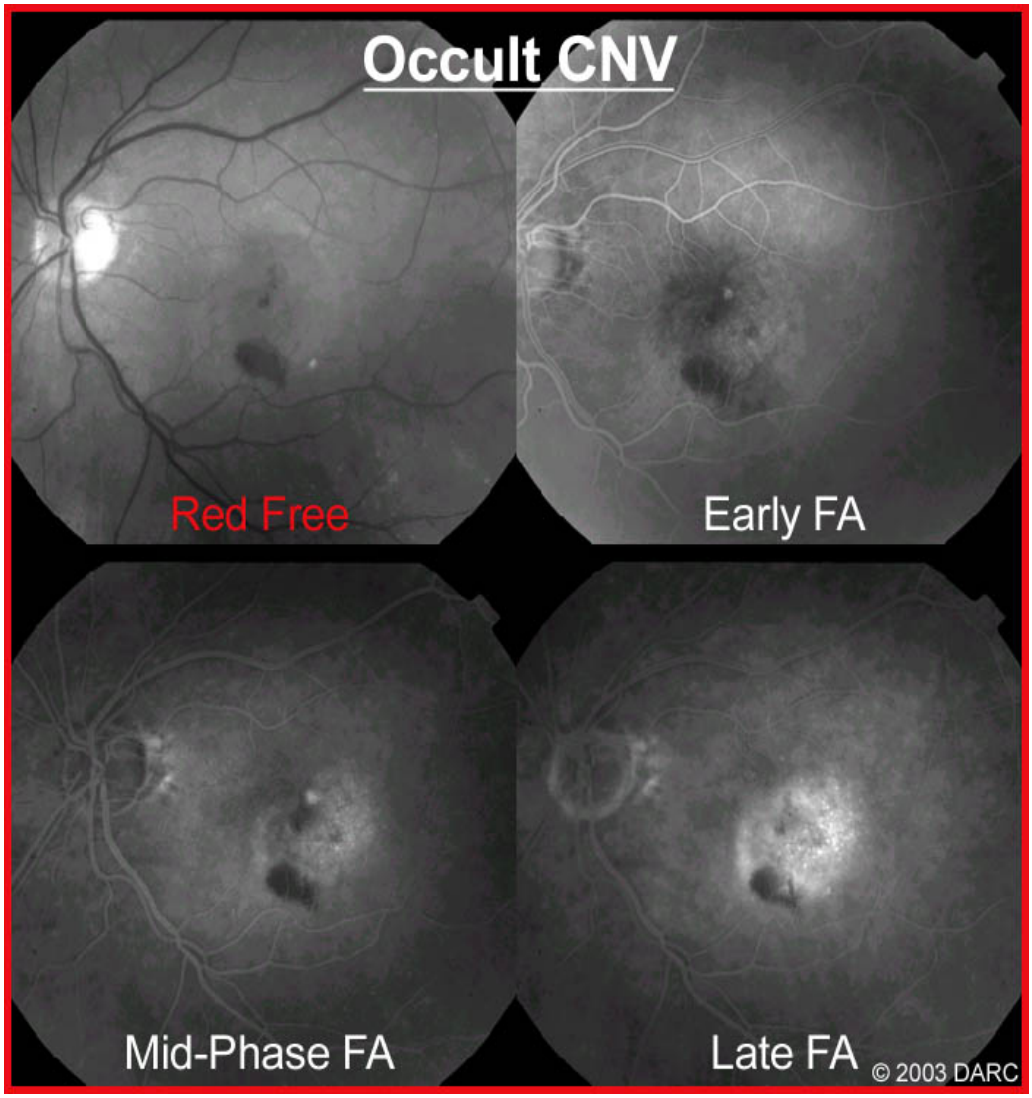
CLASSIC CNVM



Lacy pattern of hyperfluorescence in early phase

Increase intensity in mid phase.

Leaks in late phase obscuring the boundaries



Speckled hyperflouresence with dye pooled in subretinal space in late phase

Sl.No	Name	Age	Sex	Op No.	Risk factors					VN	FFA	OCT	Inj Avaastin Follow up					
					Smoking	Alchol	HT	DM	CVS				At 2 months			At 4 months		
													Vn	FFA	OCT	Vn	FFA	OCT
1	RAJESHWARI	63	F	77321	—	—	+	+	+	5/60PH6/24	+	236	6/60NIP	+	236	6/36NIP	—	236
2	RAMACHANDRAN	68	M	44671	+	—	+	—	—	1/60NIP	+	271	3/60NIP	—	241	5/60PH6/24	—	227
3	SUNDARAM	65	M	25594	+	—	+	—	+	2/60PH4/60	+	386	3/60PH5/60	+	346	5/60PH6/60	—	268
4	NAGARAJAN	58	M	54092	+	—	+	—	+	6/60PH6/36	+	242	6/36NIP	—	198	6/36PH6/24	—	138
5	WAHEDHA	57	F	35969	—	—	+	—	—	3/60PH4/60	+	312	3/60PH4/60	+	243	5/60PH6/60	+	146
6	VENKATESAN	76	M	48161	—	—	—	—	+	HM	+	344	2/60NIP	—	305	3/60NIP	—	265
7	ANNADURAI	56	M	44087	+	—	—	—	—	6/36PH6/24	+	178	6/24NIP	—	178	6/24PH6/18	—	147
8	NAVANEETHA	70	F	40607	+	—	+	—	—	1/60PH2/60	+	227	3/60NIP	+	227	6/60PH6/36	—	227
9	SATISHKUMAR	58	M	54004	+	+	—	—	—	2/60PH3/60	+	239	3/60PH4/60	—	186	5/60PH6/60	—	136
10	SENTHILRAJ	62	M	24122	+	—	—	—	+	2/60NIP	+	386	5/60NIP	+	241	6/60NIP	—	174
11	JAYALAKSHMI	58	F	47368	—	—	+	—	—	5/60PH6/24	+	244	6/60PH6/24	—	226	6/60PH6/24	—	111
12	MEENAKSHI	67	F	45682	—	—	+	—	—	1/60PH3/60	+	365	3/60PH4/60	+	276	5/60PH6/60	—	234
13	MANIKUMAR	64	M	16099	+	—	—	—	+	4/60NIP	+	228	6/60NIP	+	228	6/36NIP	—	228
14	PAULRAJ	57	M	58748	+	+	+	+	—	2/60PH4/60	+	298	5/60PH6/60	—	251	6/60PH6/36	—	193
15	KANMANI	65	F	43297	—	—	+	—	+	3/60NIP	+	240	3/60NIP	—	210	5/60NIP	+	109
16	RADHABAI	55	F	48195	—	—	—	—	+	5/60PH6/24	+	396	6/60PH6/36	+	298	6/60PH6/36	—	148
17	PONNAMBALAM	68	M	33416	+	—	+	—	—	1/60NIP	+	274	4/60NIP	—	247	6/60NIP	—	145
18	THOMAS	66	M	61817	+	—	—	—	—	4/60NIP	+	250	6/60NIP	+	220	6/60PH6/24	—	197
19	PERUMAL	60	M	85131	+	—	—	—	+	6/60NIP	+	302	6/36NIP	—	275	6/24NIP	—	209
20	CHANDRA	78	F	32528	—	—	+	—	—	1/60PH2/60	+	371	3/60PH5/60	+	289	5/60PH6/60	+	145
21	KANNAPAN	62	M	31918	+	—	—	—	+	2/60PH4/60	+	198	3/60PH4/60	—	198	5/60NIP	—	198
22	MUNUSAMY	74	M	44161	+	—	+	+	+	1/60NIP	+	316	3/60PH4/60	—	288	6/60NIP	—	148
23	SRINEVASAN	55	M	40709	+	—	—	—	+	6/60PH6/36	+	367	6/36NIP	+	279	6/36PH6/24	+	235
24	LINGAM	71	M	61218	—	+	+	+	—	1/60PH3/60	+	228	2/60PH3/60	+	209	4/60PH6/60	—	155
25	PANGAJAM	64	F	31317	—	—	+	—	—	2/60PH4/60	+	325	2/60PH4/60	—	278	4/60PH6/60	—	123
26	SHANMUGAM	69	M	42188	+	—	—	—	+	2/60NIP	+	229	3/60NIP	+	229	5/60NIP	—	174
27	MOHAN	56	M	38178	+	+	+	+	—	2/60PH3/60	+	371	4/60PH5/60	—	330	6/60PH6/36	—	157
28	SIVAKUMAR	61	M	54917	+	—	—	—	+	3/60PH4/60	+	230	4/60PH5/60	+	156	5/60PH6/60	—	156
29	VELAN	67	M	43237	+	—	+	—	—	1/60PH3/60	+	340	1/60PH3/60	—	310	4/60PH6/60	—	143
30	LOGANATHAN	59	M	56177	+	—	—	—	—	3/60NIP	+	361	6/60NIP	—	279	6/60NIP	—	214
31	KAMATCHI	66	F	44749	—	—	+	—	+	HM	+	348	2/60NIP	—	312	4/60PH5/60	—	167
32	SARADHA	55	F	42184	—	—	+	—	—	5/60PH6/24	+	350	6/60PH6/36	—	271	6/36NIP	—	147

33	KADHARBASHA	60	M	83711	+	—	+	—	—	1/60NIP	+	236	3/60PH4/60	—	200	4/60PH5/60	—	165
34	NANTHAKUMAR	65	M	48175	+	—	—	—	+	2/60PH4/60	+	295	3/60PH4/60	—	165	5/60PH6/60	—	134
35	CHINNAMAL	63	F	33563	—	—	+	—	—	6/60PH6/36	+	287	6/36NIP	+	203	6/36PH6/24	+	176
36	SIVAKUMAR	67	M	33368	—	—	+	—	+	1/60PH3/60	+	379	3/60PH5/60	—	297	5/60NIP	—	167
37	POONGODI	56	F	42193	—	—	—	—	+	5/60PH6/24	+	235	6/60NIP	—	205	6/36NIP	—	173
38	VIJAYAKUMAR	73	M	24835	+	—	+	—	—	HM	+	270	2/60NIP	+	270	5/60PH6/60	+	270
39	ARUMUGAM	62	M	33176	+	+	—	—	—	2/60PH3/60	+	383	3/60PH6/60	—	246	4/60PH6/60	—	190
40	KUMARASAMY	64	M	34197	+	—	+	—	+	2/60NIP	+	275	2/60NIP	+	234	4/60NIP	—	210
41	THANDAPANI	70	M	33490	+	—	—	—	+	3/60PH4/60	+	238	6/60NIP	—	238	6/60PH6/24	—	238
42	PRAKASH	57	M	33765	+	—	+	—	—	6/36PH6/24	+	311	6/60PH6/36	—	245	6/24NIP	—	172
43	THIYAGARAJAN	82	M	33820	+	+	—	—	—	1/60PH2/60	+	317	3/60PH5/60	—	270	5/60PH6/60	—	136
44	RADHA	61	F	43591	—	—	+	—	+	6/60NIP	+	328	6/36PH6/24	—	257	6/36PH6/24	—	217
45	RAJASEKAR	73	M	54172	+	—	+	—	+	3/60NIP	+	289	5/60NIP	+	169	6/36NIP	—	129
46	ELLAPPAN	75	M	40027	—	+	—	—	—	2/60PH4/60	+	245	5/60PH6/60	+	211	6/60PH6/24	—	153
47	KUMARESAN	69	M	43996	+	—	+	—	—	1/60NIP	+	255	3/60NIP	—	255	5/60PH6/60	—	255
48	KALAVATHI	59	F	44178	—	—	+	+	+	5/60PH6/24	+	312	5/60PH6/24	+	247	6/60NIP	—	216
49	MUTHU	66	M	32197	+	—	—	—	—	3/60NIP	+	371	5/60PH6/60	—	331	6/60PH6/24	—	156
50	SRITHAR	55	M	45498	+	—	—	—	—	6/60NIP	+	288	6/36NIP	+	168	6/36PH6/24	—	127